FIGURE 1

CCAATCGCCCGGTGCGGTGGTGCAGGGTCTCGGGCTAGTC**ATG**GCGTCCCCGTCTCGGAGAC
TGCAGACTAAACCAGTCATTACTTGTTTCAAGAGCGTTCTGCTAATCTACACTTTTATTTTC
TGGATCACTGGCGTTATCCTTCTTGCAGTTGGCATTTGGGGCAAGGTGAGCCTGGAGAATTA
CTTTTCTCTTTTAAATGAGAAGGCCACCAATGTCCCCTTCGTGCTCATTGCTACTGGTACCG
TCATTATTCTTTTGGGCACCTTTGGTTGTTTTGCTACCTGCCGAGCTTCTGCATGGATGCTA
AAACTGTATGCAATGTTTCTGACTCTCGTTTTTTTGGTCGAACTGGTCGCTGCCATCGTAGG
ATTTGTTTTCAGACATGAGATTAAGAACAGCTTTAAGAATAATTATGAGAAGGCTTTGAAGC
AGTATAACTCTACAGGAGATTATAGAAGCCATGCAGTAGACAAGATCCAAAATACGTTGCAT
TGTTGTGGTGTCACCGATTATAGAGATTGGACAGATACTAATTATTACTCAGAAAAAGGATT
TCCTAAGAGTTGCTGTAAACTTGAAGATTGTACTCCACAGAGAGATGCAGACAAAGTAAACA
ATGAAGGTTGTTTTATAAAGGTGATGACCATTATAGAGTCAGAAATGGGAGTCGTTGCAGGA
ATTTCCTTTGGAGTTGCTTGCTTCCAACTGATTGGAATCTTTCTCGCCTACTGCCWCTCTCG
TGCCATAACAAATAACCAGTATGAGATAGTG**TAA**CCCAATGTATCTGTGGGCCTATTCCTCT
CTACCTTTAAGGACATTTAGGGTCCCCCCTGTGAATTAGAAAGTTGCTTGGCTGGAGAACTG
ACAACACTACTTACTGATAGACCAAAAAACTACACCAGTAGGTTGATTCAATCAAGATGTAT
GTAGACCTAAAACTACACCAATAGGCTGATTCAATCAAGATCCGTGCTCGCAGTGGGCTGAT
TCAATCAAGATGTATGTTTGCTATGTTCTAAGTCCACCTTCTATCCCATTCATGTTAGATCG
TTGAAACCCTGTATCCCTCTGAAACACTGGAAGAGCTAGTAAATTGTAAATGAAGT

FIGURE 2

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA19902
><subunit 1 of 1, 245 aa, 1 stop, 1 unknown
><MW: -1, pI: 8.36, NX(S/T): 1
MASPSRRLQTKPVITCFKSVLLIYTFIFWITGVILLAVGIWGKVSLENYFSLLNEKATNVPF
VLIATGTVIILLGTFGCFATCRASAWMLKLYAMFLTLVFLVELVAAIVGFVFRHEIKNSFKN
NYEKALKQYNSTGDYRSHAVDKIQNTLHCCGVTDYRDWTDTNYYSEKGFPKSCCKLEDCTPQ
RDADKVNNEGCFIKVMTIIESEMGVVAGISFGVACFQLIGIFLAYCXSRAITNNQYEIV

Important features of the protein:

Signal peptide:
amino acids 1-42

Transmembrane domains:
amino acids 19-42, 61-83, 92-114, 209-230,

N-glycosylation site.
amino acids 134-138

Tyrosine kinase phosphorylation site.
amino acids 160-168, 160-169

N-myristoylation site.
amino acids 75-81, 78-84, 210-216, 214-220, 226-232

Prokaryotic membrane lipoprotein lipid attachment site.
amino acids 69-80, 211-222

FIGURE 3

CCCACGCGTCCGGCGCCGTGGCCTCGCGTCCATCTTTGCCGTTCTCTCGGACCTGTCACAAA
GGAGTCGCGCCGCCGCCGCCGCCCCCTCCCTCCGGTGGGCCCGGGAGGTAGAGAAAGTCAGT
GCCACAGCCCGACCGCGCTGCTCTGAGCCCTGGGCACGCGGAACGGGAGGGAGTCTGAGGGT
TGGGGACGTCTGTGAGGGAGGGGAACAGCCGCTCGAGCCTGGGGCGGGCGGACCGGACTGGG
GCCGGGGTAGGCTCTGGAAAGGGCCCGGGAGAGAGGTGGCGTTGGTCAGAACCTGAGAAACA
GCCGAGAGGTTTTCCACCGAGGCCCGCGCTTGAGGGATCTGAAGAGGTTCCTAGAAGAGGGT
GTTCCCTCTTTCGGGGGTCCTCACCAGAAGAGGTTCTTGGGGGTCGCCCTTCTGAGGAGGCT
GCGGCTAACAGGGCCCAGAACTGCCATTGGATGTCCAGAATCCCCTGTAGTTGATAATGTTG
GGAATAAGCTCTGCAACTTTCTTTGGCATTCAGTTGTTAAAAACAAATAGGATGCAAATTCC
TCAACTCCAGGTTATGAAAACAGTACTTGGAAAACTGAAAACTACCTAA**ATG**ATCGTCTTTG
GTTGGGCCGTGTTCTTAGCGAGCAGAAGCCTTGGCCAGGGTCTGTTGTTGACTCTCGAAGAG
CACATAGCCCACTTCCTAGGGACTGGAGGTGCCGCTACTACCATGGGTAATTCCTGTATCTG
CCGAGATGACAGTGGAACAGATGACAGTGTTGACACCCAACAGCAACAGGCCGAGAACAGTG
CAGTACCCACTGCTGACACAAGGAGCCAACCACGGGACCCTGTTCGGCCACCAAGGAGGGGC
CGAGGACCTCATGAGCCAAGGAGAAAGAAACAAAATGTGGATGGGCTAGTGTTGGACACACT
GGCAGTAATACGGACTCTTGTAGATAAG**TAA**GTATCTGACTCACGGTCACCTCCAGTGGAAT
GAAAAGTGTTCTGCCCGGAACCATGACTTTAGGACTCCTTCAGTTCCTTTAGGACATACTCG
CCAAGCCTTGTGCTCACAGGGCAAAGGAGAATATTTTAATGCTCCGCTGATGGCAGAGTAAA
TGATAAGATTTGATGTTTTTGCTTGCTGTCATCTACTTTGTCTGGAAATGTCTAAATGTTTC
TGTAGCAGAAAACACGATAAAGCTATGATCTTTATTAGAG

FIGURE 4

MIVFGWAVFLASRSLGQGLLLTLEEHIAHFLGTGGAATTMGNSCICRDDSGTDDSVDTQQQQ
AENSAVPTADTRSQPRDPVRPPRRGRGPHEPRRKKQNVDGLVLDTLAVIRTLVDKO

Signal peptide:
amino acids 1-16

Casein kinase II phosphorylation site.
amino acids 22-26, 50-54, 113-117

N-myristoylation site.
amino acids 18-24, 32-38, 34-40, 35-41, 51-57

FIGURE 5

GGCACGAGGCGCTGTCCACCCGGGGGCGTGGGAGTGAGGTACCAGATTCAGCCCATTTGGCC
CCGACGCCTCTGTTCTCGGAATCCGGGTGCTGCGGATTGAGGTCCCGGTTCCTAACGGACTG
CAAG**ATG**GAGGAAGGCGGGAACCTAGGAGGCCTGATTAAGATGGTCCATCTACTGGTCTTGT
CAGGTGCCTGGGGCATGCAAATGTGGGTGACCTTCGTCTCAGGCTTCCTGCTTTTCCGAAGC
CTTCCCCGACATACCTTCGGACTAGTGCAGAGCAAACTCTTCCCCTTCTACTTCCACATCTC
CATGGGCTGTGCCTTCATCAACCTCTGCATCTTGGCTTCACAGCATGCTTGGGCTCAGCTCA
CATTCTGGGAGGCCAGCCAGCTTTACCTGCTGTTCCTGAGCCTTACGCTGGCCACTGTCAAC
GCCCGCTGGCTGGAACCCCGCACCACAGCTGCCATGTGGGCCCTGCAAACCGTGGAGAAGGA
GCGAGGCCTGGGTGGGGAGGTACCAGGCAGCCACCAGGGTCCCGATCCCTACCGCCAGCTGC
GAGAGAAGGACCCCAAGTACAGTGCTCTCCGCCAGAATTTCTTCCGCTACCATGGGCTGTCC
TCTCTTTGCAATCTGGGCTGCGTCCTGAGCAATGGGCTCTGTCTCGCTGGCCTTGCCCTGGA
AATAAGGAGCCTC**TAG**CATGGGCCCTGCATGCTAATAAATGCTTCTTCAGAAATGAAAAAAA
AAAAAAAAAAAA

FIGURE 6

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56107

<subunit 1 of 1, 231 aa, 1 stop

<NX(S/T): 0

MEEGGNLGGLIKMVHLLVLSGAWGMQMWVTFVSGFLLFRSLPRHTFGLVQSKLFPFYFHISM
GCAFINLCILASQHAWAQLTFWEASQLYLLFLSLTLATVNARWLEPRTTAAMWALQTVEKER
GLGGEVPGSHQGPDPYRQLREKDPKYSALRQNFFRYHGLSSLCNLGCVLSNGLCLAGLALEIRSL

Signal peptide:

amino acids 1-24

Transmembrane domain:

amino acids 86-103, 60-75

Casein kinase II phosphorylation site.

amino acids 82-86

Tyrosine kinase phosphorylation site.

amino acids 144-151

N-myristoylation site.

amino acids 4-10, 5-11, 47-53, 170-176, 176-182

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 54-65

G-protein coupled receptors proteins.

amino acids 44-85

FIGURE 7

AATTCAGATTTTAAGCCCATTCTGCAGTGGAATTTCATGAACTAGCAAGAGGACACCATCTT
CTTGTATTATACAAGAAAGGAGTGTACCTATCACACACAGGGGGAAAA**ATG**CTCTTTTGGGT
GCTAGGCCTCCTAATCCTCTGTGGTTTTCTGTGGACTCGTAAAGGAAAACTAAAGATTGAAG
ACATCACTGATAAGTACATTTTTATCACTGGATGTGACTCGGGCTTTGGAAACTTGGCAGCC
AGAACTTTTGATAAAAAGGGATTTCATGTAATCGCTGCCTGTCTGACTGAATCAGGATCAAC
AGCTTTAAAGGCAGAAACCTCAGAGAGACTTCGTACTGTGCTTCTGGATGTGACCGACCCAG
AGAATGTCAAGAGGACTGCCCAGTGGGTGAAGAACCAAGTTGGGGAGAAAGGTCTCTGGGGT
CTGATCAATAATGCTGGTGTTCCCGGCGTGCTGGCTCCCACTGACTGGCTGACACTAGAGGA
CTACAGAGAACCTATTGAAGTGAACCTGTTTGGACTCATCAGTGTGACACTAAATATGCTTC
CTTTGGTCAAGAAAGCTCAAGGGAGAGTTATTAATGTCTCCAGTGTTGGAGGTCGCCTTGCA
ATCGTTGGAGGGGGCTATACTCCATCCAAATATGCAGTGGAAGGTTTCAATGACAGCTTAAG
ACGGGACATGAAAGCTTTTGGTGTGCACGTCTCATGCATTGAACCAGGATTGTTCAAAACAA
ACTTGGCAGATCCAGTAAAGGTAATTGAAAAAAAACTCGCCATTTGGGAGCAGCTGTCTCCA
GACATCAAACAACAATATGGAGAAGGTTACATTGAAAAAAGTCTAGACAAACTGAAAGGCAA
TAAATCCTATGTGAACATGGACCTCTCTCCGGTGGTAGAGTGCATGGACCACGCTCTAACAA
GTCTCTTCCCTAAGACTCATTATGCCGCTGGAAAAGATGCCAAAATTTTCTGGATACCTCTG
TCTCACATGCCAGCAGCTTTGCAAGACTTTTTATTGTTGAAACAGAAAGCAGAGCTGGCTAA
TCCCAAGGCAGTG**TGA**CTCAGCTAACCACAAATGTCTCCTCCAGGCTATGAAATTGGCCGAT
TTCAAGAACACATCTCCTTTTCAACCCCATTCCTTATCTGCTCCAACCTGGACTCATTTAGA
TCGTGCTTATTTGGATTGCAAAAGGGAGTCCCACCATCGCTGGTGGTATCCCAGGGTCCCTG
CTCAAGTTTTCTTTGAAAAGGAGGGCTGGAATGGTACATCACATAGGCAAGTCCTGCCCTGT
ATTTAGGCTTTGCCTGCTTGGTGTGATGTAAGGGAAATTGAAAGACTTGCCCATTCAAAATG
ATCTTTACCGTGGCCTGCCCCATGCTTATGGTCCCCAGCATTTACAGTAACTTGTGAATGTT
AAGTATCATCTCTTATCTAAATATTAAAAGATAAGTCAACCCAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAA

FIGURE 8

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56406
><subunit 1 of 1, 319 aa, 1 stop
><MW: 35227, pI: 8.97, NX(S/T): 3
MLFWVLGLLILCGFLWTRKGKLKIEDITDKYIFITGCDSGFGNLAARTFDKKGFHVIAACLT
ESGSTALKAETSERLRTVLLDVTDPENVKRTAQWVKNQVGEKGLWGLINNAGVPGVLAPTDW
LTLEDYREPIEVNLFGLISVTLNMLPLVKKAQGRVINVSSVGGRLAIVGGGYTPSKYAVEGF
NDSLRRDMKAFGVHVSCIEPGLFKTNLADPVKVIEKKLAIWEQLSPDIKQQYGEGYIEKSLD
KLKGNKSYVNMDLSPVVECMDHALTSLFPKTHYAAGKDAKIFWIPLSHMPAALQDFLLLKQK
AELANPKAV

Important features of the protein:

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 136-152

N-glycosylation sites.

amino acids 161-163, 187-190 and 253-256

Glycosaminoglycan attachment site.

amino acids 39-42

N-myristoylation sites.

amino acids 36-41, 42-47, 108-113, 166-171, 198-203 and 207-212

FIGURE 9

GCGGGCTGTTGACGGCGCTGCG**ATG**GCTGCCTGCGAGGGCAGGAGAAGCGGAGCTCTCGGTT
CCTCTCAGTCGGACTTCCTGACGCCGCCAGTGGGCGGGGCCCCTTGGGCCGTCGCCACCACT
GTAGTCATGTACCCACCGCCGCCGCCGCCGCCTCATCGGGACTTCATCTCGGTGACGCTGAG
CTTTGGCGAGAGCTATGACAACAGCAAGAGTTGGCGGCGGCGCTCGTGCTGGAGGAAATGGA
AGCAACTGTCGAGATTGCAGCGGAATATGATTCTCTTCCTCCTTGCCTTTCTGCTTTTCTGT
GGACTCCTCTTCTACATCAACTTGGCTGACCATTGGAAAGCTCTGGCTTTCAGGCTAGAGGA
AGAGCAGAAGATGAGGCCAGAAATTGCTGGGTTAAAACCAGCAAATCCACCCGTCTTACCAG
CTCCTCAGAAGGCGGACACCGACCCTGAGAACTTACCTGAGATTTCGTCACAGAAGACACAA
AGACACATCCAGCGGGGACCACCTCACCTGCAGATTAGACCCCCAAGCCAAGACCTGAAGGA
TGGGACCCAGGAGGAGGCCACAAAAAGGCAAGAAGCCCCTGTGGATCCCCGCCCGGAAGGAG
ATCCGCAGAGGACAGTCATCAGCTGGAGGGGAGCGGTGATCGAGCCTGAGCAGGGCACCGAG
CTCCCTTCAAGAAGAGCAGAAGTGCCCACCAAGCCTCCCCTGCCACCGGCCAGGACACAGGG
CACACCAGTGCATCTGAACTATCGCCAGAAGGGCGTGATTGACGTCTTCCTGCATGCATGGA
AAGGATACCGCAAGTTTGCATGGGGCCATGACGAGCTGAAGCCTGTGTCCAGGTCCTTCAGT
GAGTGGTTTGGCCTCGGTCTCACACTGATCGACGCGCTGGACACCATGTGGATCTTGGGTCT
GAGGAAAGAATTTGAGGAAGCCAGGAAGTGGGTGTCGAAGAAGTTACACTTTGAAAAGGACG
TGGACGTCAACCTGTTTGAGAGCACGATCCGCATCCTGGGGGGGCTCCTGAGTGCCTACCAC
CTGTCTGGGGACAGCCTCTTCCTGAGGAAAGCTGAGGATTTTGGAAATCGGCTAATGCCTGC
CTTCAGAACACCATCCAAGATTCCTTACTCGGATGTGAACATCGGTACTGGAGTTGCCCACC
CGCCACGGTGGACCTCCGACAGCACTGTGGCCGAGGTGACCAGCATTCAGCTGGAGTTCCGG
GAGCTCTCCCGTCTCACAGGGGATAAGAAGTTTCAGGAGGCAGTGGAGAAGGTGACACAGCA
CATCCACGGCCTGTCTGGGAAGAAGGATGGGCTGGTGCCCATGTTCATCAATACCCACAGTG
GCCTCTTCACCCACCTGGGCGTATTCACGCTGGGCGCCAGGGCCGACAGCTACTATGAGTAC
CTGCTGAAGCAGTGGATCCAGGGCGGGAAGCAGGAGACACAGCTGCTGGAAGACTACGTGGA
AGCCATCGAGGGTGTCAGAACGCACCTGCTGCGGCACTCCGAGCCCAGTAAGCTCACCTTTG
TGGGGGAGCTTGCCCACGGCCGCTTCAGTGCCAAGATGGACCACCTGGTGTGCTTCCTGCCA
GGGACGCTGGCTCTGGGCGTCTACCACGGCCTGCCCGCCAGCCACATGGAGCTGGCCCAGGA
GCTCATGGAGACTTGTTACCAGATGAACCGGCAGATGGAGACGGGGCTGAGTCCCGAGATCG
TGCACTTCAACCTTTACCCCCAGCCGGGCCGTCGGGACGTGGAGGTCAAGCCAGCAGACAGG
CACAACCTGCTGCGGCCAGAGACCGTGGAGAGCCTGTTCTACCTGTACCGCGTCACAGGGGA
CCGCAAATACCAGGACTGGGGCTGGGAGATTCTGCAGAGCTTCAGCCGATTCACACGGGTCC
CCTCGGGTGGCTATTCTTCCATCAACAATGTCCAGGATCCTCAGAAGCCCGAGCCTAGGGAC
AAGATGGAGAGCTTCTTCCTGGGGGAGACGCTCAAGTATCTGTTCTTGCTCTTCTCCGATGA
CCCAAACCTGCTCAGCCTGGACGCCTACGTGTTCAACACCGAAGCCCACCCTCTGCCTATCT
GGACCCCTGCC**TAG**GGTGGATGGCTGCTGGTGTGGGGACTTCGGGTGGGCAGAGGCACCTTG
CTGGGTCTGTGGCATTTTCCAAGGGCCCACGTAGCACCGGCAACCGCCAAGTGGCCCAGGCT
CTGAACTGGCTCTGGGCTCCTCCTCGTCTCTGCTTTAATCAGGACACCGTGAGGACAAGTGA
GGCCGTCAGTCTTGGTGTGATGCGGGGTGGGCTGGGCCGCTGGAGCCTCCGCCTGCTTCCTC
CAGAAGACACGAATCATGACTCACGATTGCTGAAGCCTGAGCAGGTCTCTGTGGGCCGACCA
GAGGGGGGCTTCGAGGTGGTCCCTGGTACTGGGGTGACCGAGTGGACAGCCCAGGGTGCAGC
TCTGCCCGGGCTCGTGAAGCCTCAGATGTCCCCAATCCAAGGGTCTGGAGGGGCTGCCGTGA
CTCCAGAGGCCTGAGGCTCCAGGGCTGGCTCTGGTGTTTACAAGCTGGACTCAGGGATCCTC
CTGGCCGCCCCGCAGGGGGCTTGGAGGGCTGGACGGCAAGTCCGTCTAGCTCACGGGCCCCT
CCAGTGGAATGGGTCTTTTCGGTGGAGATAAAAGTTGATTTGCTCTAACCGCAA

FIGURE 10

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56529

><subunit 1 of 1, 699 aa, 1 stop

><MW: 79553, pI: 7.83, NX(S/T): 0

MAACEGRRSGALGSSQSDFLTPPVGGAPWAVATTVVMYPPPPPPPHRDFISVTLSFGESYDN
SKSWRRRSCWRKWKQLSRLQRNMILFLLAFLLFCGLLFYINLADHWKALAFRLEEEQKMRPE
IAGLKPANPPVLPAPQKADTDPENLPEISSQKTQRHIQRGPPHLQIRPPSQDLKDGTQEEAT
KRQEAPVDPRPEGDPQRTVISWRGAVIEPEQGTELPSRRAEVPTKPPLPPARTQGTPVHLNY
RQKGVIDVFLHAWKGYRKFAWGHDELKPVSRSFSEWFGLGLTLIDALDTMWILGLRKEFEEA
RKWVSKKLHFEKDVDVNLFESTIRILGGLLSAYHLSGDSLFLRKAEDFGNRLMPAFRTPSKI
PYSDVNIGTGVAHPPRWTSDSTVAEVTSIQLEFRELSRLTGDKKFQEAVEKVTQHIHGLSGK
KDGLVPMFINTHSGLFTHLGVFTLGARADSYYEYLLKQWIQGGKQETQLLEDYVEAIEGVRT
HLLRHSEPSKLTFVGELAHGRFSAKMDHLVCFLPGTLALGVYHGLPASHMELAQELMETCYQ
MNRQMETGLSPEIVHFNLYPQPGRRDVEVKPADRHNLLRPETVESLFYLYRVTGDRKYQDWG
WEILQSFSRFTRVPSGGYSSINNVQDPQKPEPRDKMESFFLGETLKYLFLLFSDDPNLLSLD
AYVFNTEAHPLPIWTPA

Important features of the protein:

Transmembrane domain:

amino acids 21-40 and 84-105 (type II)

FIGURE 11

GGCGCCGCGTAGGCCCGGGAGGCCGGGCCGGCCGGGCTGCGAGCGCCTGCCCCATGCGCCGC

CGCCTCTCCGCACG**ATG**TTCCCCTCGCGGAGGAAAGCGGCGCAGCTGCCCTGGGAGGACGGC

AGGTCCGGGTTGCTCTCCGGCGGCCTCCCTCGGAAGTGTTCCGTCTTCCACCTGTTCGTGGC

CTGCCTCTCGCTGGGCTTCTTCTCCCTACTCTGGCTGCAGCTCAGCTGCTCTGGGGACGTGG

CCCGGGCAGTCAGGGGACAAGGGCAGGAGACCTCGGGCCCTCCCCGTGCCTGCCCCCCAGAG

CCGCCCCCTGAGCACTGGGAAGAAGACGCATCCTGGGGCCCCCACCGCCTGGCAGTGCTGGT

GCCCTTCCGCGAACGCTTCGAGGAGCTCCTGGTCTTCGTGCCCCACATGCGCCGCTTCCTGA

GCAGGAAGAAGATCCGGCACCACATCTACGTGCTCAACCAGGTGGACCACTTCAGGTTCAAC

CGGGCAGCGCTCATCAACGTGGGCTTCCTGGAGAGCAGCAACAGCACGGACTACATTGCCAT

GCACGACGTTGACCTGCTCCCTCTCAACGAGGAGCTGGACTATGGCTTTCCTGAGGCTGGGC

CCTTCCACGTGGCCTCCCCGGAGCTCCACCCTCTCTACCACTACAAGACCTATGTCGGCGGC

ATCCTGCTGCTCTCCAAGCAGCACTACCGGCTGTGCAATGGGATGTCCAACCGCTTCTGGGG

CTGGGGCCGCGAGGACGACGAGTTCTACCGGCGCATTAAGGGAGCTGGGCTCCAGCTTTTCC

GCCCCTCGGGAATCACAACTGGGTACAAGACATTTCGCCACCTGCATGACCCAGCCTGGCGG

AAGAGGGACCAGAAGCGCATCGCAGCTCAAAAACAGGAGCAGTTCAAGGTGGACAGGGAGGG

AGGCCTGAACACTGTGAAGTACCATGTGGCTTCCCGCACTGCCCTGTCTGTGGGCGGGGCCC

CCTGCACTGTCCTCAACATCATGTTGGACTGTGACAAGACCGCCACACCCTGGTGCACATTC

AGC**TGA**GCTGGATGGACAGTGAGGAAGCCTGTACCTACAGGCCATATTGCTCAGGCTCAGGA

CAAGGCCTCAGGTCGTGGGCCCAGCTCTGACAGGATGTGGAGTGGCCAGGACCAAGACAGCA

AGCTACGCAATTGCAGCCACCCGGCCGCCAAGGCAGGCTTGGGCTGGGCCAGGACACGTGGG

GTGCCTGGGACGCTGCTTGCCATGCACAGTGATCAGAGAGAGGCTGGGGTGTGTCCTGTCCG

GGACCCCCCCTGCCTTCCTGCTCACCCTACTCTGACCTCCTTCACGTGCCCAGGCCTGTGGG

TAGTGGGGAGGGCTGAACAGGACAACCTCTCATCACCCTACTCTGACCTCCTTCACGTGCCC

AGGCCTGTGGGTAGTGGGGAGGGCTGAACAGGACAACCTCTCATCACCCCCAAAAAAAAAAA

AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 12

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56531

><subunit 1 of 1, 327 aa, 1 stop

><MW: 37406, pI: 9.30, NX(S/T): 1

MFPSRRKAAQLPWEDGRSGLLSGGLPRKCSVFHLFVACLSLGFFSLLWLQLSCSGDVARAVR
GQGQETSGPPRACPPEPPPEHWEEDASWGPHRLAVLVPFRERFEELLVFVPHMRRFLSRKKI
RHHIYVLNQVDHFRFNRAALINVGFLESSNSTDYIAMHDVDLLPLNEELDYGFPEAGPFHVA
SPELHPLYHYKTYVGGILLLSKQHYRLCNGMSNRFWGWGREDDEFYRRIKGAGLQLFRPSGI
TTGYKTFRHLHDPAWRKRDQKRIAAQKQEQFKVDREGGLNTVKYHVASRTALSVGGAPCTVL
NIMLDCDKTATPWCTFS

Signal peptide:
amino acids 1-42

Transmembrane domain:
amino acids 29-49 (type II)

N-glycosylation site.
amino acids 154-158

cAMP- and cGMP-dependent protein kinase phosphorylation site.
amino acids 27-31

Tyrosine kinase phosphorylation site.
amino acids 226-233

N-myristoylation site.
amino acids 19-25, 65-71, 247-253, 285-291, 303-309, 304-310

FIGURE 13

CAATGTTTGCCTATCCACCTCCCCCAAGCCCCTTTACCT**ATG**CTGCTGCTAACGCTGCTGCT
GCTGCTGCTGCTGCTTAAAGGCTCATGCTTGGAGTGGGGACTGGTCGGTGCCCAGAAAGTCT
CTTCTGCCACTGACGCCCCCATCAGGGATTGGGCCTTCTTTCCCCCTTCCTTTCTGTGTCTC
CTGCCTCATCGGCCTGCCATGACCTGCAGCCAAGCCCAGCCCCGTGGGGAAGGGGAGAAAGT
GGGGGATGGC**TAA**GAAAGCTGGGAGATAGGGAACAGAAGAGGGTAGTGGGTGGGCTAGGGGG
GCTGCCTTATTTAAAGTGGTTGTTTATGATTCTTATACTAATTTATACAAAGATATTAAGGC
CCTGTTCATTAAGAAATTGTTCCCTTCCCCTGTGTTCAATGTTTGTAAAGATTGTTCTGTGT
AAATATGTCTTTATAATAAACAGTTAAAAGCTGAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 14

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56862

<subunit 1 of 1, 73 aa, 1 stop

<MW: 7879, pI: 7.21, NX(S/T): 0

MLLLTLLLLLLLLKGSCLEWGLVGAQKVSSATDAPIRDWAFFPPSFLCLLPHRPAMTCSQAQ

PRGEGEKVGDG

Important features:

Signal peptide:

amino acids 1-15

Growth factor and cytokines receptors family:

amino acids 3-18

FIGURE 15

GGGACCCATGCGGCCGTGACCCCCGGCTCCCTAGAGGCCCAGCGCAGCCGCAGCGGACAAAG
GAGCATGTCCGCGCCGGGGAAGGCCCGTCCTCCGGCCGCCATAAGGCTCCGGTCGCCGCTGG
GCCCGCGCCGCGCTCCTGCCCGCCCGGGCTCCGGGGCGGCCCGCTAGGCCAGTGCGCCGCCG
CTCGCCCCGCAGGCCCCGGCCCGCAGC**ATG**GAGCCACCCGGACGCCGGCGGGGCCGCGCGCA
GCCGCCGCTGTTGCTGCCGCTCTCGCTGTTAGCGCTGCTCGCGCTGCTGGGAGGCGGCGGCG
GCGGCGGCGCCGCGGCGCTGCCCGCCGGCTGCAAGCACGATGGGCGGCCCCGAGGGGCTGGC
AGGGCGGCGGGCGCCGCCGAGGGCAAGGTGGTGTGCAGCAGCCTGGAACTCGCGCAGGTCCT
GCCCCCAGATACTCTGCCCAACCGCACGGTCACCCTGATTCTGAGTAACAATAAGATATCCG
AGCTGAAGAATGGCTCATTTTCTGGGTTAAGTCTCCTTGAAAGATTGGACCTCCGAAACAAT
CTTATTAGTAGTATAGATCCAGGTGCCTTCTGGGGACTGTCATCTCTAAAAAGATTGGATCT
GACAAACAATCGAATAGGATGTCTGAATGCAGACATATTTCGAGGACTCACCAATCTGGTTC
GGCTAAACCTTTCGGGGAATTTGTTTTCTTCATTATCTCAAGGAACTTTTGATTATCTTGCG
TCATTACGGTCTTTGGAATTCCAGACTGAGTATCTTTTGTGTGACTGTAACATACTGTGGAT
GCATCGCTGGGTAAAGGAGAAGAACATCACGGTACGGGATACCAGGTGTGTTTATCCTAAGT
CACTGCAGGCCCAACCAGTCACAGGCGTGAAGCAGGAGCTGTTGACATGCGACCCTCCGCTT
GAATTGCCGTCTTTCTACATGACTCCATCTCATCGCCAAGTTGTGTTTGAAGGAGACAGCCT
TCCTTTCCAGTGCATGGCTTCATATATTGATCAGGACATGCAAGTGTTGTGGTATCAGGATG
GGAGAATAGTTGAAACCGATGAATCGCAAGGTATTTTTGTTGAAAAGAACATGATTCACAAC
TGCTCCTTGATTGCAAGTGCCCTAACCATTTCTAATATTCAGGCTGGATCTACTGGAAATTG
GGGCTGTCATGTCCAGACCAAACGTGGGAATAATACGAGGACTGTGGATATTGTGGTATTAG
AGAGTTCTGCACAGTACTGTCCTCCAGAGAGGGTGGTAAACAACAAAGGTGACTTCAGATGG
CCCAGAACATTGGCAGGCATTACTGCATATCTGCAGTGTACGCGGAACACCCATGGCAGTGG
GATATATCCCGGAAACCCACAGGATGAGAGAAAAGCTTGGCGCAGATGTGATAGAGGTGGCT
TTTGGGCAGATGATGATTATTCTCGCTGTCAGTATGCAAATGATGTCACTAGAGTTCTTTAT
ATGTTTAATCAGATGCCCCTCAATCTTACCAATGCCGTGGCAACAGCTCGACAGTTACTGGC
TTACACTGTGGAAGCAGCCAACTTTTCTGACAAAATGGATGTTATATTTGTGGCAGAAATGA
TTGAAAAATTTGGAAGATTTACCAAGGAGGAAAAATCAAAAGAGCTAGGTGACGTGATGGTT
GACATTGCAAGTAACATCATGTTGGCTGATGAACGTGTCCTGTGGCTGGCGCAGAGGGAAGC
TAAAGCCTGCAGTAGGATTGTGCAGTGTCTTCAGCGCATTGCTACCTACCGGCTAGCCGGTG
GAGCTCACGTTTATTCAACATATTCACCCAATATTGCTCTGGAAGCTTATGTCATCAAGTCT
ACTGGCTTCACGGGGATGACCTGTACCGTGTTCCAGAAAGTGGCAGCCTCTGATCGTACAGG
ACTTTCGGATTATGGGAGGCGGGATCCAGAGGGAAACCTGGATAAGCAGCTGAGCTTTAAGT
GCAATGTTTCAAATACATTTTCGAGTCTGGCACTAAAGGTATGTTACATTCTGCAATCATTT
AAGACTATTTACAGT**TAA**ATTAGAATGCTCCAAATGTTCTGCTTCGCAAAATAACCTTATTA
AAAGATTTTTTTTTGCAGGAAGATAGGTATTATTGCTTTTGCTACTGTTTTAAAGAAAACTA
ACCAGGAAGAACTGCATTACGACTTTCAAGGGCCCTAGGCATTTTTGCCTTTGATTCCCTTT
CTTCACATAAAAATATCAGAAATTACATTTTATAACTGCAGTGGTATAAATGCAAATATACT
ATTGTTACATGTGAAAAAATTTTATTTGACTTAAAAGTTTATTTATTTGTTTTTTTGCTCCT
GATTTTAAGACAATAAGATGTTTTCATGGGCCCCTAAAAGTATCATGAGCCTTTGGCACTGC
GCCTGCCAAGCCTAGTGGAGAAGTCAACCCTGAGACCAGGTGTTTAATCAAGCAAGCTGTAT
ATCAAAATTTTTGGCAGAAAACACAAATATGTCATATATCTTTTTTTAAAAAAAGTATTTCA
TTGAAGCAAGCAAAATGAAAGCATTTTTACTGATTTTTAAAATTGGTGCTTTAGATATATTT
GACTACACTGTATTGAAGCAAATAGAGGAGGCACAACTCCAGCACCCTAATGGAACCACATT
TTTTTCACTTAGCTTTCTGTGGGCATGTGTAATTGTATTCTCTGCGGTTTTTAATCTCACAG
TACTTTATTTCTGTCTTGTCCCTCAATAATATCACAAACAATATTCCAGTCATTTTAATGGC
TGCATAATAACTGATCCAACAGGTGTTAGGTGTTCTGGTTTAGTGTGAGCACTCAATAAATA
TTGAATGAATGAACGAAAAAAAAAAAAAAAAA

FIGURE 16

MEPPGRRRGRAQPPLLLPLSLLALLALLGGGGGGGAAALPAGCKHDGRPRGAGRAAGAAEGK
VVCSSLELAQVLPPDTLPNRTVTLILSNNKISELKNGSFSGLSLLERLDLRNNLISSIDPGA
FWGLSSLKRLDLTNNRIGCLNADIFRGLTNLVRLNLSGNLFSSLSQGTFDYLASLRSLEFQT
EYLLCDCNILWMHRWVKEKNITVRDTRCVYPKSLQAQPVTGVKQELLTCDPPLELPSFYMTP
SHRQVVFEGDSLPFQCMASYIDQDMQVLWYQDGRIVETDESQGIFVEKNMIHNCSLIASALT
ISNIQAGSTGNWGCHVQTKRGNNTRTVDIVVLESSAQYCPPERVVNNKGDFRWPRTLAGITA
YLQCTRNTHGSGIYPGNPQDERKAWRRCDRGGFWADDDYSRCQYANDVTRVLYMFNQMPLNL
TNAVATARQLLAYTVEAANFSDKMDVIFVAEMIEKFGRFTKEEKSKELGDVMVDIASNIMLA
DERVLWLAQREAKACSRIVQCLQRIATYRLAGGAHVYSTYSPNIALEAYVIKSTGFTGMTCT
VFQKVAASDRTGLSDYGRRDPEGNLDKQLSFKCNVSNTFSSLALKVCYILQSFKTIYS

Signal peptide:

amino acids 1-33

Transmembrane domain:

amino acids 13-40 (type II)

N-glycosylation site.

amino acids 81-85, 98-102, 159-163, 206-210, 301-305, 332-336, 433-437, 453-457, 592-596

N-myristoylation site.

amino acids 29-35, 30-36, 31-37, 32-38, 33-39, 34-40, 51-57, 57-63, 99-105, 123-129, 142-148, 162-168, 317-323, 320-326, 384-390, 403-409, 554-560

FIGURE 17

GCGTGGGG**ATG**TCTAGGAGCTCGAAGGTGGTGCTGGGCCTCTCGGTGCTGCTGACGGCGGCC

ACAGTGGCCGGCGTACATGTGAAGCAGCAGTGGGACCAGCAGAGGCTTCGTGACGGAGTTAT

CAGAGACATTGAGAGGCAAATTCGGAAAAAAGAAAACATTCGTCTTTTGGGAGAACAGATTA

TTTTGACTGAGCAACTTGAAGCAGAAAGAGAGAAGATGTTATTGGCAAAAGGATCTCAAAAA

TCA**TGA**CTTGAATGTGAAATATCTGTTGGACAGACAACACGAGTTTGTGTGTGTGTTGAT

GGAGAGTAGCTTAGTAGTATCTTCATCTTTTTTTTTGGTCACTGTCCTTTTAAACTTGATCA

AATAAAGGACAGTGGGTCATATAAGTTACTGCTTTCAGGGTCCCTTATATCTGAATAAAGGA

GTGTGGGCAGACACTTTTTGGAAGAGTCTGTCTGGGTGATCCTGGTAGAAGCCCCATTAGGG

TCACTGTCCAGTGCTTAGGGTTGTTACTGAGAAGCACTGCCGAGCTTGTGAGAAGGAAGGGA

TGGATAGTAGCATCCACCTGAGTAGTCTGATCAGTCGGCATGATGACGAAGCCACGAGAACA

TCGACCTCAGAAGGACTGGAGGAAGGTGAAGTGGAGGGAGAGACGCTCCTGATCGTCGAATCC

FIGURE 18

MSRSSKVVLGLSVLLTAATVAGVHVKQQWDQQRLRDGVIRDIERQIRKKENIRLLGEQIILT
EQLEAEREKMLLAKGSQKS

Signal peptide:

amino acids 1-21

FIGURE 19

CTGTCGTCTTTGCTTCAGCCGCAGTCGCCACTGGCTGCCTGAGGTGCTCTTACAGCCTGTTC
CAAGTGTGGCTTAATCCGTCTCCACCACCAGATCTTTCTCCGTGGATTCCTCTGCTAAGACC
GCTGCC**ATG**CCAGTGACGGTAACCCGCACCACCATCACAACCACCACGACGTCATCTTCGGG
CCTGGGGTCCCCCATGATCGTGGGGTCCCCTCGGGCCCTGACACAGCCCCTGGGTCTCCTTCGC
CTGCTGCAGCTGGTGTCTACCTGCGTGGCCTTCTCGCTGGTGGCTAGCGTGGGCGCCTGGAC
GGGGTCCATGGGCAACTGGTCCATGTTCACCTGGTGCTTCTGCTTCTCCGTGACCCTGATCA
TCCTCATCGTGGAGCTGTGCGGGCTCCAGGCCCGCTTCCCCCTGTCTTGGCGCAACTTCCCC
ATCACCTTCGCCTGCTATGCGGCCCTCTTCTGCCTCTCGGCCTCCATCATCTACCCCACCAC
CTATGTCCAGTTCCTGTCCCACGGCCGTTCGCGGGACCACGCCATCGCCGCCACCTTCTTCT
CCTGCATCGCGTGTGTGGCTTACGCCACCGAAGTGGCCTGGACCCGGGCCCGGCCCGGCGAG
ATCACTGGCTATATGGCCACCGTACCCGGGCTGCTGAAGGTGCTGGAGACCTTCGTTGCCTG
CATCATCTTCGCGTTCATCAGCGACCCCAACCTGTACCAGCACCAGCCGGCCCTGGAGTGGT
GCGTGGCGGTGTACGCCATCTGCTTCATCCTAGCGGCCATCGCCATCCTGCTGAACCTGGGG
GAGTGCACCAACGTGCTACCCATCCCCTTCCCCAGCTTCCTGTCGGGGCTGGCCTTGCTGTC
TGTCCTCCTCTATGCCACCGCCCTTGTTCTCTGGCCCCTCTACCAGTTCGATGAGAAGTATG
GCGGCCAGCCTCGGCGCTCGAGAGATGTAAGCTGCAGCCGCAGCCATGCCTACTACGTGTGT
GCCTGGGACCGCCGACTGGCTGTGGCCATCCTGACGGCCATCAACCTACTGGCGTATGTGGC
TGACCTGGTGCACTCTGCCCACCTGGTTTTTGTCAAGGTC**TAA**GACTCTCCCAAGAGGCTCC
CGTTCCCTCTCCAACCTCTTTGTTCTTCTTGCCCGAGTTTTCTTTATGGAGTACTTCTTTCC
TCCGCCTTTCCTCTGTTTTCCTCTTCCTGTCTCCCCTCCCTCCCACCTTTTTCTTTCCTTCC
CAATTCCTTGCACTCTAACCAGTTCTTGGATGCATCTTCTTCCTTCCCTTTCCTCTTGCTGT
TTCCTTCCTGTGTTGTTTTGTTGCCCACATCCTGTTTTCACCCCTGAGCTGTTTCTCTTTTT
CTTTTCTTTCTTTTTTTTTTTTTTTTTAAGACGGATTCTCACTCTGTGGCCCAGGCTGGAG
TGCAGTGGTGCGATCTCAGCTCACTGCAACCCCCGCCTCCTGGGTTCAAGCGATTCTCCTCC
CCCAGCCTCCCAAGTAGCTGGGAGGACAGGTGTGAGCTGCCGCACCCAGCCTGTTTCTCTTT
TTCCACTCTTCTTTTTTCTCATCTCTTTTCTGGGTTGCCTGTCGGCTTTCTTATCTGCCTGT
TTTGCAAGCACCTTCTCCTGTGTCCTTGGGAGCCCTGAGACTTCTTTCTCTCCTTGCCTCCA
CCCACCTCCAAAGGTGCTGAGCTCACATCCACACCCCTTGCAGCCGTCCATGCCACAGCCCC
CCAAGGGGCCCCATTGCCAAAGCATGCCTGCCCACCCTCGCTGTGCCTTAGTCAGTGTGTAC
GTGTGTGTGTGTGTGTGTTTGGGGGGTGGGGGGTGGGTAGCTGGGGATTGGGCCCTCTTTCT
CCCAGTGGAGGAAGGTGTGCAGTGTACTTCCCCTTTAAATTAAAAAACATATATATATATAT
ATTTGGAGGTCAGTAATTTCCAATGGGCGGGAGGCATTAAGCACCGACCCTGGGTCCCTAGG
CCCCGCCTGGCACTCAGCCTTGCCAGAGATTGGCTCCAGAATTTTTGCCAGGCTTACAGAACAC
CCACTGCCTAGAGGCCATCTTAAAGGAAGCAGGGGCTGGATGCCTTTCATCCCAACTATTCT
CTGTGGTATGAAAAAG

FIGURE 20

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58727

<subunit 1 of 1, 322 aa, 1 stop

<MW: 35274, pI: 8.57, NX(S/T): 1

MPVTVTRTTITTTTTSSSGLGSPMIVGSPRALTQPLGLLRLLQLVSTCVAFSLVASVGAWTG
SMGNWSMFTWCFCFSVTLIILIVELCGLQARFPLSWRNFPITFACYAALFCLSASIIYPTTY
VQFLSHGRSRDHAIAATFFSCIACVAYATEVAWTRARPGEITGYMATVPGLLKVLETFVACI
IFAFISDPNLYQHQPALEWCVAVYAICFILAAIAILLNLGECTNVLPIPFPSFLSGLALLSV
LLYATALVLWPLYQFDEKYGGQPRRSRDVSCSRSHAYYVCAWDRRLAVAILTAINLLAYVAD
LVHSAHLVFVKV

Important features:

Transmembrane domains:

amino acids 41-60 (type II), 66-85, 101-120, 137-153, 171-192, 205-226, 235-255 and 294-312

N-glycosylation site.

amino acids 66-69

Glycosaminoglycan attachment site.

amino acids 18-21

FIGURE 21

GAACGTGCCACCATGCCCAGCTAATTTTTGTATTTTTAGTAGAGACGGGGTTTCACCATGTTGGCCAGGCTGGTC
TTGAACTCGTGACCTCATGATCCGCTCACCTCGGCCTCCCAAAGTGCTGGGATTACAGGCATGAGCCACTGACGC
CTGGCCAGCCTATGCATTTTTAAGAAATTATTCTGTATTAGGTGCTGTGCTAAACATTGGGCACTACAGTGACCA
AAACAGACTGAATTCCCCAAGAGCCAAAGACCAGTGAGGGAGACCAACAAGAAACAGGAAATGCAAAAGAGACCA
TTATTACTCACTATGACTAAGGGTCACAAATGGGGTACGTTGATGGAGAGTGATTTGTTAAGAGACTACAGAGGG
AGGACAGACTACCAAGAGGGGGGCCAGGAAAGCTCCTCTGACGAGGTGGTATTTCAGCCCAAACTGGAAGAATGA
GAAAGAGCTAGCCAGCCATCAGAATAGTCCAGAAGAGATGGGGAGCACTACACTCACTACACTTTGGCCTGAGAA
AATAGCATGGGATTGGAGGAGGCTGGGGGAACACCACTTCTGCCGACCTGGGCAGGAGGCATTGAGGGCTTGAGA
AAGGGCAATGGCAGTAGCAGTAGAAAGGACAGGGTAGGAGCAGGGACTTTGCAGGTGGAATCATTAGGTCTTATC
AACAGATATGGGCAAGCAAAGCCAGGGGAGAATTGATGGTAATGCTGAGGTTTGGAGCCAGGCTAGATGGGACAG
TGGTGGGTGATGCAAAGGAAAGAGGTCAGGAAGCAGGGCCAGACGTGGGGAGAAGGTGTGGGGGTTTGGTTTCCA
TCTTGCCGAGTCTGCCGGAATGTGGATGGGAAGACCAAGAGGAGGAGCAAGGGGCAGAGGGGAAGGGAATCTTAA
AGAAGTCCTGGATGCCACACTCTTCTTCCTTCCTCCTCTTCCCTCTCCTCAGAGGTCTCACTCGTGGTTCTTCAT
TTCCTGCCCTGCCTCCATCTCCTCTGGGTGCTGGGAAAGTGGAGGATTAGCTGAAGTTTTGCTTCTCGGGGCCTG
TCTGAATCTCCATTGCTTTCTGGGAGGACATAATTCACCTGTCCTAGCTTCTTATCATCTTACATTTCCCTGTAG
CCACTGGGACATATGTGGTGTTCCTTCCTAGCTCCTGTCTCCTCCTCATGCCTTTGCTGGGTATGGGCATGTTAG
GGGGAAGGTCATTGCTGTCAGAGGGGCACTGACTTTCTAATGGTGTTACCCAAGGTGAATGTTGGAGACACAGTC
GCGATGCTGCCCAAGTCCCGGCGAGCCCTAACTATCCAGGAGATCGCTGCGCTGGCCAGGTCCTCCCTGCATGGT
ATGCAGCCCCTCCC**ATG**TTTCTGGCCACTTTGTCCTTTCTCCTCCCGTTTGCACATCCCTTTGGAACTGTTTCCT
GTGAGTACATGCTGGGGTCTCCCCTTTCTTCCCTTGCTCAGGTGAATCTCAGCCCCTTCTCCCACCCAAAGGTTC
ACATGGATCCTAACTACTGCCACCCTTCCACCTCCCTGCACCTGTGCTCCCTGGCCTGGTCCTTTACCAGGCTTC
TCCACCCTCCCCTATCTCCAGGTATTTCCCAGGTGGTGAAGGACCACGTGACCAAGCCTACCGCCATGGCCCAGG
GCCGAGTGGCTCACCTCATTGAGTGGAAGGGCTGGAGCAAGCCGAGTGACTCACCTGCTGCCCTGGAATCAGCCT
TTTCCTCCTATTCAGACCTCAGCGAGGGCGAACAAGAGGCTCGCTTTGCAGCAGGAGTGGCTGAGCAGTTTGCCA
TCGCGGAAGCCAAGCTCCGAGCATGGTCTTCGGTGGATGGCGAGGACTCCACTGATGACTCCTATGATGAGGACT
TTGCTGGGGGAATGGACACAGACATGGCTGGGCAGCTGCCCCTGGGGCCGCACCTCCAGGACCTGTTCACCGGCC
ACCGGTTCTCCCGGCCTGTGCGCCAGGGCTCCGTGGAGCCTGAGAGCGACTGCTCACAGACCGTGTCCCCAGACA
CCCTGTGCTCTAGTCTGTGCAGCCTGGAGGATGGGTTGTTGGGCTCCCCGGCCCGGCTGGCCTCCCAGCTGCTGG
GCGATGAGCTGCTTCTCGCCAAACTGCCCCCCAGCCGGGAAAGTGCCTTCCGCAGCCTGGGCCCACTGGAGGCCC
AGGACTCACTCTACAACTCGCCCCTCACAGAGTCCTGCCTTTCCCCCGCGGAGGAGGAGCCAGCCCCCTGCAAGG
ACTGCCAGCCACTCTGCCCACCACTAACGGGCAGCTGGGAACGGCAGCGGCAAGCCTCTGACCTGGCCTCTTCTG
GGGTGGTGTCCTTAGATGAGGATGAGGCAGAGCCAGAGGAACAG**TGA**CCCACATCATGCCTGGCAGTGGCATGCA
TCCCCCGGCTGCTGCCAGGGGCAGAGCCTCTGTGCCCAAGTGTGGGCTCAAGGCTCCCAGCAGAGCTCCACAGCC
TAGAGGGCTCCTGGGAGCGCTCGCTTCTCCGTTGTGTGTTTTGCATGAAAGTGTTTGGAGAGGAGGCAGGGGCTG
GGCTGGGGGCGCATGTCCTGCCCCCACTCCCGGGGCTTGCCGGGGGTTGCCCGGGGCCTCTGGGGCATGGCTACA
GCTGTGGCAGACAGTGATGTTCATGTTCTTAAAATGCCACACACACATTTCCTCCTCGGATAATGTGAACCACTA
AGGGGGTTGTGACTGGGCTGTGTGAGGGTGGGGTGGGAGGGGGCCCAGCAACCCCCCACCCTCCCCATGCCTCTC
TCTTCTCTGCTTTTCTTCTCACTTCCGAGTCCATGTGCAGTGCTTGATAGAATCACCCCCACCTGGAGGGGCTGG
CTCCTGCCCTCCCGGAGCCTATGGGTTGAGCCGTCCCTCAAGGGCCCCTGCCCAGCTGGGCTCGTGCTGTGCTTC
ATTCACCTCTCCATCGTCTCTAAATCTTCCTCTTTTTTCCTAAAGACAGAAGGTTTTTGGTCTGTTTTTTCAGTC
GGATCTTCTCTTCTCTGGGAGGCTTTGGAATGATGAAAGCATGTACCCTCCACCCTTTTCCTGGCCCCCTAATGG
GGCCTGGGCCCTTTCCCAACCCCTCCTAGGATGTGCGGGCAGTGTGCTGGCGCCTCACAGCCAGCCGGGCTGCCC
ATTCACGCAGAGCTCTCTGAGCGGGAGGTGGAAGAAAGGATGGCTCTGGTTGCCACAGAGCTGGGACTTCATGTT
CTTCTAGAGAGGGCCACAAGAGGGCCACAGGGGTGGCCGGGAGTTGTCAGCTGATGCCTGCTGAGAGGCAGGAAT
TGTGCCAGTGAGTGACAGTCATGAGGGAGTGTCTCTTCTTGGGGAGGAAAGAAGGTAGAGCCTTTCTGTCTGAAT
GAAAGGCCAAGGCTACAGTACAGGGCCCCGCCCCAGCCAGGGTGTTAATGCCCACGTAGTGGAGGCCTCTGGCAG
ATCCTGCATTCCAAGGTCACTGGACTGTACGTTTTTATGGTTGTGGGAAGGGTGGGTGGCTTTAGAATTAAGGGC
CTTGTAGGCTTTGGCAGGTAAGAGGGCCCAAGGTAAGAACGAGAGCCAACGGGCACAAGCATTCTATATATAAGT
GGCTCATTAGGTGTTTATTTTGTTCTATTTAAGAATTTGTTTTATTAAATTAATATAAAAATCTTTGTAAATCTC
TAAAA

FIGURE 22

MFLATLSFLLPFAHPFGTVSCEYMLGSPLSSLAQVNLSPFSHPKVHMDPNYCHPSTSLHLCS
LAWSFTRLLHPPLSPGISQVVKDHVTKPTAMAQGRVAHLIEWKGWSKPSDSPAALESAFSSY
SDLSEGEQEARFAAGVAEQFAIAEAKLRAWSSVDGEDSTDDSYDEDFAGGMDTDMAGQLPLG
PHLQDLFTGHRFSRPVRQGSVEPESDCSQTVSPDTLCSSLCSLEDGLLGSPARLASQLLGDE
LLLAKLPPSRESAFRSLGPLEAQDSLYNSPLTESCLSPAEEEPAPCKDCQPLCPPLTGSWER
QRQASDLASSGVVSLDEDEAEPEEQ

Signal peptide:

amino acids 1-15

Casein kinase II phosphorylation site.

amino acids 123-127, 128-132, 155-159, 162-166, 166-170, 228-232, 285-289, 324-328

Tyrosine kinase phosphorylation site.

amino acids 44-52

N-myristoylation site.

amino acids 17-23, 26-32, 173-179

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 11-22

FIGURE 23

GGTTCCTGGGCGCTCTGTTACACAAGCAAGATACAGCCAGCCCCACCTAATTTTGTTTCCCT
GGCACCCTCCTGCTCAGTGCGACATTGTCACACTTAACCCATCTGTTTTCTCTAATGCACGA
CAGATTCCTTTCAGACAGGACAACTGTGATATTTCAGTTCCTGATTGTAAATACCTCCTAAG
CCTGAAGCTTCTGTTACTAGCCATTGTGAGCTTCAGTTTCTTCATCTGCAAAATGGGCATAA
TACAATCTATTCTTGCCACATCAAGGGATTGTTATTCCTTTAAAAAAAAACCAATACCAAAG
AAGCCTACA**ATG**TTGGCCTTAGCCAAAATTCTGTTGATTTCAACGTTGTTTTATTCACTTCT
ATCGGGGAGCCATGGAAAAGAAAATCAAGACATAAACACAACACAGAACATTGCAGAAGTTT
TTAAAACAATGGAAAATAAACCTATTTCTTTGGAAAGTGAAGCAAACTTAAACTCAGATAAA
GAAAATATAACCACCTCAAATCTCAAGGCGAGTCATTCCCCTCCTTTGAATCTACCCAACAA
CAGCCACGGAATAACAGATTTCTCCAGTAACTCATCAGCAGAGCATTCTTTGGGCAGTCTAA
AACCCACATCTACCATTTCCACAAGCCCTCCCTTGATCCATAGCTTTGTTTCTAAAGTGCCT
TGGAATGCACCTATAGCAGATGAAGATCTTTTGCCCATCTCAGCACATCCCAATGCTACACC
TGCTCTGTCTTCAGAAAACTTCACTTGGTCTTTGGTCAATGACACCGTGAAAACTCCTGATA
ACAGTTCCATTACAGTTAGCATCCTCTCTTCAGAACCAACTTCTCCATCTGTGACCCCCTTG
ATAGTGGAACCAAGTGGATGGCTTACCACAAACAGTGATAGCTTCACTGGGTTTACCCCTTA
TCAAGAAAAAACAACTCTACAGCCTACCTTAAAATTCACCAATAATTCAAAACTCTTTCCAA
ATACGTCAGATCCCCAAAAAGAAAATAGAAATACAGGAATAGTATTCGGGGCCATTTTAGGT
GCTATTCTGGGTGTCTCATTGCTTACTCTTGTGGGCTACTTGTTGTGGAAAAAGGAAAAC
GGATTCATTTTCCCATCGGCGACTTTATGACGACAGAAATGAACCAGTTCTGCGATTAGACA
ATGCACCGGAACCTTATGATGTGAGTTTTGGGAATTCTAGCTACTACAATCCAACTTTGAAT
GATTCAGCCATGCCAGAAAGTGAAGAAAATGCACGTGATGGCATTCCTATGGATGACATACC
TCCACTTCGTACTTCTGTA**TAG**AACTAACAGCAAAAAGGCGTTAAACAGCAAGTGTCATCTA
CATCCTAGCCTTTTGACAAATTCATCTTTCAAAAGGTTACACAAAATTACTGTCACGTGGAT
TTTGTCAAGGAGAATCATAAAAGCAGGAGACCAGTAGCAGAAATGTAGACAGGATGTATCAT
CCAAAGGTTTTCTTTCTTACAATTTTTGGCCATCCTGAGGCATTTACTAAGTAGCCTTAATT
TGTATTTTAGTAGTATTTTCTTAGTAGAAAATATTTGTGGAATCAGATAAAACTAAAAGATT
TCACCATTACAGCCCTGCCTCATAACTAAATAATAAAAATTATTCCACCAAAAAATTCTAAA
ACAATGAAGATGACTCTTTACTGCTCTGCCTGAAGCCCTAGTACCATAATTCAAGATTGCAT
TTTCTTAAATGAAAATTGAAAGGGTGCTTTTTAAAGAAAATTTGACTTAAAGCTAAAAAGAG
GACATAGCCCAGAGTTTCTGTTATTGGGAAATTGAGGCAATAGAAATGACAGACCTGTATTC
TAGTACGTTATAATTTTCTAGATCAGCACACACATGATCAGCCCACTGAGTTATGAAGCTGA
CAATGACTGCATTCAACGGGGCCATGGCAGGAAAGCTGACCCTACCCAGGAAAGTAATAGCT
TCTTTAAAAGTCTTCAAAGGTTTTGGGAATTTTAACTTGTCTTAATATATCTTAGGCTTCAA
TTATTTGGGTGCCTTAAAAACTCAATGAGAATCATGGT

FIGURE 24

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58732
><subunit 1 of 1, 334 aa, 1 stop
><MW: 36294, pI: 4.98, NX(S/T): 13
MLALAKILLISTLFYSLLSGSHGKENQDINTTQNIAEVFKTMENKPISLESEANLNSDKENI
TTSNLKASHSPPLNLPNNSHGITDFSSNSSAEHSLGSLKPTSTISTSPPLIHSFVSKVPWNA
PIADEDLLPISAHPNATPALSSENFTWSLVNDTVKTPDNSSITVSILSSEPTSPSVTPLIVE
PSGWLTTNSDSFTGFTPYQEKTTLQPTLKFTNNSKLFPNTSDPQKENRNTGIVFGAILGAIL
GVSLLTLVGYLLCGKRKTDSFSHRRLYDDRNEPVLRLDNAPEPYDVSFGNSSYYNPTLNDSA
MPESEENARDGIPMDDIPPLRTSV

Signal peptide:
amino acids 1-23

Transmembrane domain:
amino acids 235-262

N-glycosylation site.
amino acids 30-34, 61-65, 79-83, 90-94, 148-152, 155-159, 163-167, 218-222, 225-229, 298-302, 307-311

FIGURE 25

AACAGGATCTCCTCTTGCAGTCTGCAGCCCAGGACGCTGATTCCAGCAGCGCCTTACCGCGC
AGCCCGAAGATTCACT**ATG**GTGAAAATCGCCTTCAATACCCCTACCGCCGTGCAAAAGGAGG
AGGCGCGGCAAGACGTGGAGGCCCTCCTGAGCCGCACGGTCAGAACTCAGATACTGACCGGC
AAGGAGCTCCGAGTTGCCACCCAGGAAAAAGAGGGCTCCTCTGGGAGATGTATGCTTACTCT
CTTAGGCCTTTCATTCATCTTGGCAGGACTTATTGTTGGTGGAGCCTGCATTTACAAGTACT
TCATGCCCAAGAGCACCATTTACCGTGGAGAGATGTGCTTTTTTGATTCTGAGGATCCTGCA
AATTCCCTTCGTGGAGGAGAGCCTAACTTCCTGCCTGTGACTGAGGAGGCTGACATTCGTGA
GGATGACAACATTGCAATCATTGATGTGCCTGTCCCCAGTTTCTCTGATAGTGACCCTGCAG
CAATTATTCATGACTTTGAAAAGGGAATGACTGCTTACCTGGACTTGTTGCTGGGGAACTGC
TATCTGATGCCCCTCAATACTTCTATTGTTATGCCTCCAAAAAATCTGGTAGAGCTCTTTGG
CAAACTGGCGAGTGGCAGATATCTGCCTCAAACTTATGTGGTTCGAGAAGACCTAGTTGCTG
TGGAGGAAATTCGTGATGTTAGTAACCTTGGCATCTTTATTTACCAACTTTGCAATAACAGA
AAGTCCTTCCGCCTTCGTCGCAGAGACCTCTTGCTGGGTTTCAACAAACGTGCCATTGATAA
ATGCTGGAAGATTAGACACTTCCCCAACGAATTTATTGTTGAGACCAAGATCTGTCAAGAG**T**
AAGAGGCAACAGATAGAGTGTCCTTGGTAATAAGAAGTCAGAGATTTACAATATGACTTTAA
CATTAAGGTTTATGGATACTCAAGATATTTACTCATGCATTTACTCTATTGCTTATGCTTT
AAAAAAAGGAAAAAAAAAAAAAACTACTAACCACTGCAAGCTCTTGTCAAATTTTAGTTTAAT
TGGCATTGCTTGTTTTTTGAAACTGAAATTACATGAGTTTCATTTTTTCTTTGCATTTATAG
GGTTTAGATTTCTGAAAGCAGCATGAATATATCACCTAACATCCTGACAATAAATTCCATCC
GTTGTTTTTTTTGTTTGTTTGTTTTTTCTTTTCCTTTAAGTAAGCTCTTTATTCATCTTATG
GTGGAGCAATTTTAAAATTTGAAATATTTTAAATTGTTTTTGAACTTTTTGTGTAAAATATA
TCAGATCTCAACATTGTTGGTTTCTTTTGTTTTTCATTTTGTACAACTTTCTTGAATTTAGA
AATTACATCTTTGCAGTTCTGTTAGGTGCTCTGTAATTAACCTGACTTATATGTGAACAATT
TTCATGAGACAGTCATTTTTAACTAATGCAGTGATTCTTTCTCACTACTATCTGTATTGTGG
AATGCACAAAATTGTGTAGGTGCTGAATGCTGTAAGGAGTTTAGGTTGTATGAATTCTACAA
CCCTATAATAAATTTTACTCTATACAAAAAAAAAAAAAAAAAAA

FIGURE 26

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58828
<subunit 1 of 1, 263 aa, 1 stop
<MW: 29741, pI: 5.74, NX(S/T): 1

MVKIAFNTPTAVQKEEARQDVEALLSRTVRTQILTGKELRVATQEKEGSSGRCMLTLLGLSF
ILAGLIVGGACIYKYFMPKSTIYRGEMCFFDSEDPANSLRGGEPNFLPVTEEADIREDDNIA
IIDVPVPSFSDSDPAAIIHDFEKGMTAYLDLLLGNCYLMPLNTSIVMPPKNLVELFGKLASG
RYLPQTYVVREDLVAVEEIRDVSNLGIFIYQLCNNRKSFRLRRRDLLLGFNKRAIDKCWKIR
HFPNEFIVETKICQE

Type II transmembrane domain:
amino acids 53-75

N-glycosylation site.
amino acids 166-170

Casein kinase II phosphorylation site.
amino acids 35-39, 132-136, 134-138

N-myristoylation site.
amino acids 66-72, 103-109

Prokaryotic membrane lipoprotein lipid attachment site.
amino acids 63-74

FIGURE 27

GGAGGAGGGAGGGCGGGCAGGCGCCAGCCCAGAGCAGCCCCGGGCACCAGCACGGACTCTCT
CTTCCAGCCCAGGTGCCCCCCACTCTCGCTCCATTCGGCGGGAGCACCCAGTCCTGTACGCC
AAGGAACTGGTCCTGGGGGCACC**ATG**GTTTCGGCGGCAGCCCCCAGCCTCCTCATCCTTCTG
TTGCTGCTGCTGGGGTCTGTGCCTGCTACCGACGCCCGCTCTGTGCCCCTGAAGGCCACGTT
CCTGGAGGATGTGGCGGGTAGTGGGGAGGCCGAGGGCTCGTCGGCCTCCTCCCCGAGCCTCC
CGCCACCCTGGACCCCGGCCCTCAGCCCCACATCGATGGGGCCCCAGCCCACAACCCTGGGG
GGCCCATCACCCCCCACCAACTTCCTGGATGGGATAGTGGACTTCTTCCGCCAGTACGTGAT
GCTGATTGCTGTGGTGGGCTCCCTGGCCTTTCTGCTGATGTTCATCGTCTGTGCCGCGGTCA
TCACCCGGCAGAAGCAGAAGGCCTCGGCCTATTACCCATCGTCCTTCCCCAAGAAGAAGTAC
GTGGACCAGAGTGACCGGGCCGGGGGCCCCCGGGCCTTCAGTGAGGTCCCCGACAGAGCCCC
CGACAGCAGGCCCGAGGAAGCCCTGGATTCCTCCCGGCAGCTCCAGGCCGACATCTTGGCCG
CCACCCAGAACCTCAAGTCCCCCACCAGGGCTGCACTGGGCGGTGGGGACGGAGCCAGGATG
GTGGAGGGCAGGGGCGCAGAGGAAGAGGAGAAGGGCAGCCAGGAGGGGGACCAGGAAGTCCA
GGGACATGGGGTCCCAGTGGAGACACCAGAGGCGCAGGAGGAGCCGTGCTCAGGGGTCCTTG
AGGGGGCTGTGGTGGCCGGTGAGGGCCAAGGGGAGCTGGAAGGGTCTCTCTTGTTAGCCCAG
GAAGCCCAGGGACCAGTGGGTCCCCCCGAAAGCCCCTGTGCTTGCAGCAGTGTCCACCCCAG
TGTC**TAA**CAGTCCTCCCGGGCTGCCAGCCCTGACTGTCGGGCCCCCAAGTGGTCACCTCCCC
GTGTATGAAAAGGCCTTCAGCCCTGACTGCTTCCTGACACTCCCTCCTTGGCCTCCCTGTGG
TGCCAATCCCAGCATGTGCTGATTCTACAGCAGGCAGAAATGCTGGTCCCCGGTGCCCCGGA
GGAATCTTACCAAGTGCCATCATCCTTCACCTCAGCAGCCCCAAAGGGCTACATCCTACAGC
ACAGCTCCCCTGACAAAGTGAGGGAGGGCACGTGTCCCTGTGACAGCCAGGATAAAACATCC
CCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGTGCCCGGCCCAAACTACTTTTTAAAACA
GCTACAGGGTAAAATCCTGCAGCACCCACTCTGGAAAATACTGCTCTTAATTTTCCTGAAGG
TGGCCCCCTGTTTCTAGTTGGTCCAGGATTAGGGATGTGGGGTATAGGGCATTTAAATCCTC
TCAAGCGCTCTCCAAGCACCCCCGGCCTGGGGGTGAGTTTCTCATCCCGCTACTGCTGCTGG
GATCAGGTTGAATGAATGGAACTCTTCCTGTCTGGCCTCCAAAGCAGCCTAGAAGCTGAGGG
GCTGTGTTTGAGGGGACCTCCACCCTGGGGAAGTCCGAGGGGCTGGGGAAGGGTTTCTGACG
CCCAGCCTGGAGCAGGGGGGCCCTGGCCACCCCCTGTTGCTCACACATTGTCTGGCAGCCTG
TGTCCACAATATTCGTCAGTCCTCGACAGGGAGCCTGGGCTCCGTCCTGCTTTAGGGAGGCT
CTGGCAGGAGGTCCTCTCCCCCATCCCTCCATCTGGGGCTCCCCCAACCTCTGCACAGCTCT
CCAGGTGCTGAGATATAATGCACCAGCACAATAAACCTTTATTCCGGCCTGAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGA

FIGURE 28

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58852

><subunit 1 of 1, 283 aa, 1 stop

><MW: 29191, pI: 4.52, NX(S/T): 0

MVSAAAPSLLILLLLLLLGSVPATDARSVPLKATFLEDVAGSGEAEGSSASSPSLPPPWTPAL
SPTSMGPQPTTLGGPSPPTNFLDGIVDFFRQYVMLIAVVGSLAFLLMFIVCAAVITRQKQKA
SAYYPSSFPKKKYVDQSDRAGGPRAFSEVPDRAPDSRPEEALDSSRQLQADILAATQNLKSP
TRAALGGGDGARMVEGRGAEEEEKGSQEGDQEVQGHGVPVETPEAQEEPCSGVLEGAVVAGE
GQGELEGSLLLAQEAQGPVGPPESPCACSSVHPSV

Signal peptide:

amino acids 1-25

Transmembrane domain:

amino acids 94-118

N-myristoylation site.

amino acids 18-24, 40-46, 46-52, 145-151, 192-198, 193-199, 211-217, 238-244, 242-248

FIGURE 29

GTGGACTCTGAGAAGCCCAGGCAGTTGAGGACAGGAGAGAGAAGGCTGCAGACCCAGAGGGA
GGGAGGACAGGGAGTCGGAAGGAGGAGGACAGAGGAGGGCACAGAGACGCAGAGCAAGGGCG
GCAAGGAGGAGACCCTGGTGGGAGGAAGACACTCTGGAGAGAGAGGGGGCTGGGCAGAG**ATG**
AAGTTCCAGGGGCCCCTGGCCTGCCTCCTGCTGGCCCTCTGCCTGGGCAGTGGGGAGGCTGG
CCCCCTGCAGAGCGGAGAGGAAAGCACTGGGACAAATATTGGGGAGGCCCTTGGACATGGCC
TGGGAGACGCCCTGAGCGAAGGGGTGGGAAAGGCCATTGGCAAAGAGGCCGGAGGGGCAGCT
GGCTCTAAAGTCAGTGAGGCCCTTGGCCAAGGGACCAGAGAAGCAGTTGGCACTGGAGTCAG
GCAGGTTCCAGGCTTTGGCGCAGCAGATGCTTTGGGCAACAGGGTCGGGGAAGCAGCCCATG
CTCTGGGAAACACTGGGCACGAGATTGGCAGACAGGCAGAAGATGTCATTCGACACGGAGCA
GATGCTGTCCGCGGCTCCTGGCAGGGGGTGCCTGGCCACAGTGGTGCTTGGGAAACTTCTGG
AGGCCATGGCATCTTTGGCTCTCAAGGTGGCCTTGGAGGCCAGGGCCAGGGCAATCCTGGAG
GTCTGGGGACTCCGTGGGTCCACGGATACCCCGGAAACTCAGCAGGCAGCTTTGGAATGAAT
CCTCAGGGAGCTCCCTGGGGTCAAGGAGGCAATGGAGGGCCACCAAACTTTGGGACCAACAC
TCAGGGAGCTGTGGCCCAGCCTGGCTATGGTTCAGTGAGAGCCAGCAACCAGAATGAAGGGT
GCACGAATCCCCCACCATCTGGCTCAGGTGGAGGCTCCAGCAACTCTGGGGGAGGCAGCGGC
TCACAGTCGGGCAGCAGTGGCAGTGGCAGCAATGGTGACAACAACAATGGCAGCAGCAGTGG
TGGCAGCAGCAGTGGCAGCAGCAGTGGCAGCAGCAGTGGCGGCAGCAGTGGCGGCAGCAGTG
GTGGCAGCAGTGGCAACAGTGGTGGCAGCAGAGGTGACAGCGGCAGTGAGTCCTCCTGGGGA
TCCAGCACCGGCTCCTCCTCCGGCAACCACGGTGGGAGCGGCGGAGGAAATGGACATAAACC
CGGGTGTGAAAAGCCAGGGAATGAAGCCCGCGGGAGCGGGGAATCTGGGATTCAGGGCTTCA
GAGGACAGGGAGTTTCCAGCAACATGAGGGAAATAAGCAAAGAGGGCAATCGCCTCCTTGGA
GGCTCTGGAGACAATTATCGGGGGCAAGGGTCGAGCTGGGGCAGTGGAGGAGGTGACGCTGT
TGGTGGAGTCAATACTGTGAACTCTGAGACGTCTCCTGGGATGTTTAACTTTGACACTTTCT
GGAAGAATTTTAAATCCAAGCTGGGTTTCATCAACTGGGATGCCATAAACAAGGACCAGAGA
AGCTCTCGCATCCCG**TGA**CCTCCAGACAAGGAGCCACCAGATTGGATGGGAGCCCCCACACT
CCCTCCTTAAAACACCACCCTCTCATCACTAATCTCAGCCCTTGCCCTTGAAATAAACCTTA
GCTGCCCCACAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 30

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59212

><subunit 1 of 1, 440 aa, 1 stop

><MW: 42208, pI: 6.36, NX(S/T): 1

MKFQGPLACLLLALCLGSGEAGPLQSGEESTGTNIGEALGHGLGDALSEGVGKAIGKEAGGA
AGSKVSEALGQGTREAVGTGVRQVPGFGAADALGNRVGEAAHALGNTGHEIGRQAEDVIRHG
ADAVRGSWQGVPGHSGAWETSGGHGIFGSQGGLGGQGQGNPGGLGTPWVHGYPGNSAGSFGM
NPQGAPWGQGGNGGPPNFGTNTQGAVAQPGYGSVRASNQNEGCTNPPPSGSGGGSSNSGGGS
GSQSGSSGSGSNGDNNNGSSSGGSSSGSSSGSSSGGSSGGSSGGSSGGSSGNSGGSRGDSGSESSW
GSSTGSSSGNHGGSGGGNGHKPGCEKPGNEARGSGESGIQGFRGQGVSSNMREISKEGNRLL
GGSGDNYRGQGSSWGSGGGDAVGGVNTVNSETSPGMFNFDTFWKNFKSKLGFINWDAINKDQ
RSSRIP

Signal peptide:

amino acids 1-21

N-glycosylation site.

amino acids 265-269

Glycosaminoglycan attachment site.

amino acids 235-239, 237-241, 244-248, 255-259, 324-328, 388-392

Casein kinase II phosphorylation site.

amino acids 26-30, 109-113, 259-263, 300-304, 304-308

N-myristoylation site.

amino acids 17-23, 32-38, 42-48, 50-56, 60-66, 61-67, 64-70, 74-80, 90-96, 96-102, 130-136, 140-146, 149-155, 152-158, 155-161, 159-165, 163-169, 178-184, 190-196, 194-200, 199-205, 218-224, 236-242, 238-244, 239-245, 240-246, 245-251, 246-252, 249-252, 253-259, 256-262, 266-272, 270-276, 271-277, 275-281, 279-285, 283-289, 284-290, 287-293, 288-294, 291-297, 292-298, 295-301, 298-304, 305-311, 311-317, 315-321, 319-325, 322-328, 323-329, 325-331, 343-349, 354-360, 356-362, 374-380, 381-387, 383-389, 387-393, 389-395, 395-401

Cell attachment sequence.

amino acids 301-304

FIGURE 31

GACCGGTCCCTCCGGTCCTGGATGTGCGGACTCTGCTGCAGCGAGGGCTGCAGGCCCGCCGGGCGGTGCTCACCG
TGCCCTGGCTGGTGGAGTTTCTCTCCTTTGCTGACCATGTTGTTCCCTTGCTGGAATATTACCGGGACATCTTCA
CTCTCCTGCTGCGCCTGCACCGGAGCTTGGTGTTGTCGCAGGAGAGTGAGGGGAAG**ATG**TGTTTCCTGAACAAGC
TGCTGCTACTTGCTGTCCTGGGCTGGCTTTTCCAGATTCCCACAGTCCCTGAGGACTTGTTCTTTCTGGAAGAGG
GTCCCTCATATGCCTTTGAGGTGGACACAGTAGCCCCAGAGCATGGCTTGGACAATGCGCCTGTGGTGGACCAGC
AGCTGCTCTACACCTGCTGCCCCTACATCGGAGAGCTCCGGAAACTGCTCGCTTCGTGGGTGTCAGGCAGTAGTG
GACGGAGTGGGGGCTTCATGAGGAAAATCACCCCCACCACTACCACCAGCCTGGGAGCCCAGCCTTCCCAGACCA
GCCAGGGGCTGCAGGCACAGCTCGCCCAGGCCTTTTTCCACAACCAGCCGCCCTCCTTGCGCCGGACCGTAGAGT
TCGTGGCAGAAAGAATTGGATCAAACTGTGTCAAACATATCAAGGCTACACTGGTGGCAGATCTGGTGCGCCAGG
CAGAGTCACTTCTCCAAGAGCAGCTGGTGACACAGGGAGAGGAAGGGGGAGACCCAGCCCAGCTGTTGGAGATCT
TGTGTTCCCAGCTGTGCCCTCACGGGGCCCAGGCATTGGCCCTGGGGCGGGAGTTCTGTCAAAGGAAGAGCCCTG
GGGCTGTGCGGGCGCTGCTTCCAGAGGAGACCCCGGCAGCCGTTCTGAGCAGTGCAGAGAACATTGCTGTGGGGC
TTGCAACAGAGAAAGCCTGTGCTTGGCTGTCAGCCAACATCACAGCACTGATCAGGAGGGAGGTGAAAGCAGCAG
TGAGTCGCACACTTCGAGCCCAGGGTCCTGAACCTGCTGCCCGGGGGGAGCGGAGGGGCTGCTCCCGCGCC**TGA**C
GTGCTCTCCTTGGCCGTGGGGCCACGGGACCCTGACGAGGGAGTCTCCCCAGAGCATCTGGAACAGCTCCTAGGC
CAGCTGGGCCAGACGCTGCGGTGCCGCCAGTTCCTGTGCCCACCTGCTGAGCAGCATCTGGCAAAGTGCTCTGTG
GAGTTAGCTTCCCTCCTCGTTGCAGATCAAATTCCTATCCTAGGGCCCCCGGCACAGTACAGGCTGGAGAGAGGG
CAGGCTCGAAGGCTTCTGCACATGCTGCTTTCCTTGTGGAAGGAAGACTTTCAGGGGCCGGTTCCGCTGCAGCTG
CTGCTGAGCCCAAGAAATGTGGGGCTTCTGGCAGACACAAGGCCAAGGGAGTGGGACTTGCTGCTATTCTTGCTA
CGGGAGCTGGTGGAGAAGGGTCTGATGGGACGGATGGAGATAGAGGCCTGCCTGGGCAGCCTCCACCAGGCCCAG
TGGCCAGGGGACTTTGCTGAAGAATTAGCAACACTGTCTAATCTGTTTCTAGCCGAGCCCCACCTGCCAGAACCC
CAGCTAAGAGCCTGTGAGTTGGTGCAGCCAAACCGGGGCACTGTGCTGGCCCAGAGCTAGGGCTGAGAAGTGGCC
CTGCCTTGGGCATTGCACCAGAACCCTGGACCCCCGCCTCACGAGGAGGCCCAAGTGCCCAATGCAGACCCTCAC
TGGTTGGGGTGTAGCTGGGTCTACAGTCAGACTTCCTGCTCTAAGGGTGTCACTGCCTGGCATCCCACCACGCGA
ATCCTAGAGGAAGGAGAGTTGGCCTGATTTGGGATTATGGCAGAAAAGTCCAGAGATGCCAGTCCTGGAGTAGAA
GAGGTGGTGTTTGTTTATCTCTTGGATACTAAATGAAATGAGGTGTGTGGGCTTGTCAACACAGAATTCAAGCCT
CATTTGCTATCCCAGCATCTCTTAAAACTTTGTAGTCTTGGAATTCATGACAGAGGCAAATGACTCCTGCTTAAC
TTATGAAGAAAGTTAAAACATGAATCTTGGGAGTCTACATTTTCTTATCACCAGGAGCTGGACTGCCATCTCCTT
ATAAATGCCTAACACAGGCCGGGTCTGGTGGCTCATGCCTGTAATCCCAGCACTTTGAGAGGCCTGAGGTCGGCG
GACTGCCTGAGGTCAGGAATTCAAGACCAGCCTGGCCAACATGGCAAAACCCCATCTCTACTAAAAATAAAAAA
TTATTAGCTGGGCATGGTGGTGTGTGCCTGTAATCCCAGCTACTCAGGAGGATGAGGCAGGAGACCTGCTTGAAC
CTGGAGGTGGAGGTTGCAGTGAGCCGAGGTCGCACCACTGCACTCCAGTCTGGGTAACAGAGCGAGACTTTCTAG
AAAAAGCCTAACAAACAGATAAGGTAGGACTCAACCAACTGAAACCTGACTTTCCCCCTGTACCTTCAGCCCCTG
TGCAGGTAGTAACCTCTTGAGACCTCTCCCTGACCAGGGACCAAGCACAGGGCATTTAGAGCTTTTTAGAATAAA
CTGGTTTTCTTTAAAAAAAAAAAAAAAAAAAAGGGCGGCCGCCCTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT
TTTTTTTTTTTTTTTTAAAAAGGGCTTTTATTAAAATTCTCCCCACACGATGGCTCCTGCAATCTGCCACAGCTC
TGGGGCGTGTCCTGTAGGGAAAGGCCCTGTTTTCCCTGAGGCGGGGCTGGGCTTGTCCATGGGTCCGCGGAGCTG
GCCGTGCTTGGCGCCCTGGCGTGTGTCTAGCTGCTTCTTGCCGGGCACAGAGCTGCGGGGTCTGGGGGCACCGGG
AGCTAAGAGCAGGCTCTGGTGCAGGGGTGGAGGCCTGTCTCTTAACCGACACCCTGAGGTGCTCCTGAGATGCTG
GGTCCACCCTGAGTGGCACGGGGAGCAGCTGTGGCCGGTGCTCCTTCYTAGGCCAGTCCTGGGGAAACTAAGCTC
GGGCCCTTCTTTGCAAAGACCGAGGATGGGGTGGGTGTGGGGGACTCATGGGGAATGGCCTGAGGAGCTACGTGT
GAAGAGGGCGCCGGTTTGTTGGCTGCAGCGGCCTGGAGCGCCTCTCTCCTGAGCCTCAGTTTCCCTTTCCGTCTA
ATGAAGAACATGCCGTCTCGGTGTCTCAGGGCTATTAGGACTTGCCCTCAGGAAGTGGCCTTGGACGAGCGTCAT
GTTATTTTCACAACTGTCCTGCGACGTTGGCCTGGGCACGTCATGGAATGGCCCATGTCCCTCTGCTGCGTGGAC
GTCGCGGTCGGGAGTGCGCAGCCAGAGGCGGGGCCAGACGTGCGCCTGGGGGTGAGGGGAGGCGCCCCGGGAGGG
CCTCACAGGAAGTTGGGCTCCCGCACCACCAGGCAGGGCGGGCTCCCGCCGCCGCCGCCGCCACCACCGTCCAGG
GGCCGGTAGACAAAGTGGAAGTCGCGCTTGGGCTCGCTGCGCAGCAGGTAGCCCTTGATGCAGTGCGGCAGCGCG
TCGTCCGCCAGCTGGAAGCAGCGCCCGTCCACCAGCACGAACAGCCGGTGCGCCT

FIGURE 32

MCFLNKLLLLAVLGWLFQIPTVPEDLFFLEEGPSYAFEVDTVAPEHGLDNAPVVDQQLLYTC
CPYIGELRKLLASWVSGSSGRSGGFMRKITPTTTTSLGAQPSQTSQGLQAQLAQAFFHNQPP
SLRRTVEFVAERIGSNCVKHIKATLVADLVRQAESLLQEQLVTQGEEGGDPAQLLEILCSQL
CPHGAQALALGREFCQRKSPGAVRALLPEETPAAVLSSAENIAVGLATEKACAWLSANITAL
IRREVKAAVSRTLRAQGPEPAARGERRGCSRA

Signal peptide:
amino acids 1-18

N-glycosylation site.
amino acids 244-248

cAMP- and cGMP-dependent protein kinase phosphorylation site.
amino acids 89-93

Casein kinase II phosphorylation site.
amino acids 21-25, 167-171, 223-227

N-myristoylation site.
amino acids 100-106, 172-178, 207-213

Microbodies C-terminal targeting signal.
amino acids 278-282

FIGURE 33

TCCCTTGACAGGTCTGGTGGCTGGTTCGGGGTCTACTGAAGGCTGTCTTGATCAGGAAACTG
AAGACTCTCTGCTTTTGCCACAGCAGTTCCTGCAGCTTCCTTGAGGTGTGAACCCACATCCC
TGCCCCCAGGGCCACCTGCAGGACGCCGACACCTACCCCTCAGCAGACGCCGGAGAGAA**<u>ATG</u>**
AGTAGCAACAAAGAGCAGCGGTCAGCAGTGTTCGTGATCCTCTTTGCCCTCATCACCATCCT
CATCCTCTACAGCTCCAACAGTGCCAATGAGGTCTTCCATTACGGCTCCCTGCGGGGCCGTA
GCCGCCGACCTGTCAACCTCAAGAAGTGGAGCATCACTGACGGCTATGTCCCCATTCTCGGC
AACAAGACACTGCCCTCTCGGTGCCACCAGTGTGTGATTGTCAGCAGCTCCAGCCACCTGCT
GGGCACCAAGCTGGGCCCTGAGATCGAGCGGGCTGAGTGTACAATCCGCATGAATGATGCAC
CCACCACTGGCTACTCAGCTGATGTGGGCAACAAGACCACCTACCGCGTCGTGGCCCATTCC
AGTGTGTTCCGCGTGCTGAGGAGGCCCCAGGAGTTTGTCAACCGGACCCCTGAAACCGTGTT
CATCTTCTGGGGGCCCCCGAGCAAGATGCAGAAGCCCCAGGGCAGCCTCGTGCGTGTGATCC
AGCGAGCGGGCCTGGTGTTCCCCAACATGGAAGCATATGCCGTCTCTCCCGGCCGCATGCGG
CAATTTGACGACCTCTTCCGGGGTGAGACGGGCAAGGACAGGGAGAAGTCTCATTCGTGGTT
GAGCACAGGCTGGTTTACCATGGTGATCGCGGTGGAGTTGTGTGACCACGTGCATGTCTATG
GCATGGTCCCCCCCAACTACTGCAGCCAGCGGCCCCGCCTCCAGCGCATGCCCTACCACTAC
TACGAGCCCAAGGGGCCGGACGAATGTGTCACCTACATCCAGAATGAGCACAGTCGCAAGGG
CAACCACCACCGCTTCATCACCGAGAAAAGGGTCTTCTCATCGTGGGCCCAGCTGTATGGCA
TCACCTTCTCCCACCCCTCCTGGACC**<u>TAG</u>**GCCACCCAGCCTGTGGGACCTCAGGAGGGTCAG
AGGAGAAGCAGCCTCCGCCCAGCCGCTAGGCCAGGGACCATCTTCTGGCCAATCAAGGCTTG
CTGGAGTGTCTCCCAGCCAATCAGGGCCTTGAGGAGGATGTATCCTCCAGCCAATCAGGGCC
TGGGGAATCTGTTGGCGAATCAGGGATTTGGGAGTCTATGTGGTTAATCAGGGGTGTCTTTC
TTGTGCAGTCAGGGTCTGCGCACAGTCAATCAGGGTAGAGGGGGTATTTCTGAGTCAATCTG
AGGCTAAGGACATGTCCTTTCCCATGAGGCCTTGGTTCAGAGCCCCAGGAATGGACCCCCCA
ATCACTCCCCACTCTGCTGGGATAATGGGGTCCTGTCCCAAGGAGCTGGGAACTTGGTGTTG
CCCCCTCAATTTCCAGCACCAGAAAGAGAGATTGTGTGGGGGTAGAAGCTGTCTGGAGGCCC
GGCCAGAGAATTTGTGGGGTTGTGGAGGTTGTGGGGGCGGTGGGGAGGTCCCAGAGGTGGGA
GGCTGGCATCCAGGTCTTGGCTCTGCCCTGAGACCTTGGACAAACCCTTCCCCCTCTCTGGG
CACCCTTCTGCCCACACCAGTTTCCAGTGCGGAGTCTGAGACCCTTTCCACCTCCCCTACAA
GTGCCCTCGGGTCTGTCCTCCCCGTCTGGACCCTCCCAGCCACTATCCCTTGCTGGAAGGCT
CAGCTCTTTGGGGGGTCTGGGGTGACCTCCCCACCTCCTGGAAAACTTTAGGGTATTTTTGC
GCAAACTCCTTCAGGGTTGGGGGACTCTGAAGGAAACGGGACAAAACCTTAAGCTGTTTTCT
TAGCCCCTCAGCCAGCTGCCATTAGCTTGGCTCTTAAAGGGCCAGGCCTCCTTTTCTGCCCT
CTAGCAGGGAGGTTTTCCAACTGTTGGAGGCGCCTTTGGGGCTGCCCCTTTGTCTGGAGTCA
CTGGGGGCTTCCGAGGGTCTCCCTCGACCCTCTGTCGTCCTGGGATGGCTGTCGGGAGCTGT
ATCACCTGGGTTCTGTCCCCTGGCTCTGTATCAGGCACTTTATTAAAGCTGGGCCTCAGTGG
GGTGTGTTTGTCTCCTGCTCTTCTGGAGCCTGGAAGGAAAGGGCTTCAGGAGGAGGCTGTGA
GGCTGGAGGGACCAGATGGAGGAGGCCAGCAGCTAGCCATTGCACACTGGGGTGATGGGTGG
GGGCGGTGACTGCCCCAGACTTGGTTTTGTAATGATTTGTACAGGAATAAACACACCTACGC
TCCGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 34

MSSNKEQRSAVFVILFALITILILYSSNSANEVFHYGSLRGRSRRPVNLKKWSITDGYVPIL
GNKTLPSRCHQCVIVSSSSHLLGTKLGPEIERAECTIRMNDAPTTGYSADVGNKTTYRVVAH
SSVFRVLRRPQEFVNRTPETVFIFWGPPSKMQKPQGSLVRVIQRAGLVFPNMEAYAVSPGRM
RQFDDLFRGETGKDREKSHSWLSTGWFTMVIAVELCDHVHVYGMVPPNYCSQRPRLQRMPYH
YYEPKGPDECVTYIQNEHSRKGNHHRFITEKRVFSSWAQLYGITFSHPSWT

Signal peptide:
amino acids 1-29

Transmembrane domain:
amino acids 9-31 (type II)

N-glycosylation site.
amino acids 64-68, 115-119

cAMP- and cGMP-dependent protein kinase phosphorylation site.
amino acids 50-54

Casein kinase II phosphorylation site.
amino acids 3-7, 29-33, 53-57, 197-201

Tyrosine kinase phosphorylation site.
amino acids 253-262

N-myristoylation site.
amino acids 37-43, 114-120, 290-294

FIGURE 35

GTTTCTCATAGTTGGCGTCTTCTAAAGGAAAAACACTAAAATGAGGAACTCAGCGGACCGGGAGCGACGCAGCTT
GAGGGAAGCATCCCTAGCTGTTGGCGCAGAGGGGCGAGGCTGAAGCCGAGTGGCCCGAGGTGTCTGAGGGGCTGG
GGCAAAGGTGAAAGAGTTTCAGAACAAGCTTCCTGGAACCCATGACCCATGAAGTCTTGTCGACATTTATACCGT
CTGAGGGTAGCAGCTCGAAACTAGAAGAAGTGGAGTGTTGCCAGGGACGGCAGTATCTCTTTGTGTGACCCTGGC
GGCCTATGGGACGTTGGCTTCAGACCTTTGTGATACACC**ATG**CTGCGTGGGACGATGACGGCGTGGAGAGGAATG
AGGCCTGAGGTCACACTGGCTTGCCTCCTCCTAGCCACAGCAGGCTGCTTTGCTGACTTGAACGAGGTCCCTCAG
GTCACCGTCCAGCCTGCGTCCACCGTCCAGAAGCCCGGAGGCACTGTGATCTTGGGCTGCGTGGTGGAACCTCCA
AGGATGAATGTAACCTGGCGCCTGAATGGAAAGGAGCTGAATGGCTCGGATGATGCTCTGGGTGTCCTCATCACC
CACGGGACCCTCGTCATCACTGCCCTTAACAACCACACTGTGGGACGGTACCAGTGTGTGGCCCGGATGCCTGCG
GGGGCTGTGGCCAGCGTGCCAGCCACTGTGACACTAGCCAATCTCCAGGACTTCAAGTTAGATGTGCAGCACGTG
ATTGAAGTGGATGAGGGAAACACAGCAGTCATTGCCTGCCACCTGCCTGAGAGCCACCCCAAAGCCCAGGTCCGG
TACAGCGTCAAACAAGAGTGGCTGGAGGCCTCCAGAGGTAACTACCTGATCATGCCCTCAGGGAACCTCCAGATT
GTGAATGCCAGCCAGGAGGACGAGGGCATGTACAAGTGTGCAGCCTACAACCCAGTGACCCAGGAAGTGAAAACC
TCCGGCTCCAGCGACAGGCTACGTGTGCGCCGCTCCACCGCTGAGGCTGCCCGCATCATCTACCCCCCAGAGGCC
CAAACCATCATCGTCACCAAAGGCCAGAGTCTCATTCTGGAGTGTGTGGCCAGTGGAATCCCACCCCCACGGGTC
ACCTGGGCCAAGGATGGGTCCAGTGTCACCGGCTACAACAAGACGCGCTTCCTGCTGAGCAACCTCCTCATCGAC
ACCACCAGCGAGGAGGACTCAGGCACCTACCGCTGCATGGCCGACAATGGGGTTGGGCAGCCCGGGGCAGCGGTC
ATCCTCTACAATGTCCAGGTGTTTGAACCCCCTGAGGTCACCATGGAGCTATCCCAGCTGGTCATCCCCTGGGGC
CAGAGTGCCAAGCTTACCTGTGAGGTGCGTGGGAACCCCCCGCCCTCCGTGCTGTGGCTGAGGAATGCTGTGCCC
CTCATCTCCAGCCAGCGCCTCCGGCTCTCCCGCAGGGCCCTGCGCGTGCTCAGCATGGGGCCTGAGGACGAAGGC
GTCTACCAGTGCATGGCCGAGAACGAGGTTGGGAGCGCCCATGCCGTAGTCCAGCTGCGGACCTCCAGGCCAAGC
ATAACCCCAAGGCTATGGCAGGATGCTGAGCTGGCTACTGGCACACCTCCTGTATCACCCTCCAAACTCGGCAAC
CCTGAGCAGATGCTGAGGGGGCAACCGGCGCTCCCCAGACCCCCAACGTCAGTGGGGCCTGCTTCCCCGAAGTGT
CCAGGAGAGAAGGGGCAGGGGGCTCCCGCCGAGGCTCCCATCATCCTCAGCTCGCCCCGCACCTCCAAGACAGAC
TCATATGAACTGGTGTGGCGGCCTCGGCATGAGGGCAGTGGCCGGGCGCCAATCCTCTACTATGTGGTGAAACAC
CGCAAGCAGGTCACAAATTCCTCTGACGATTGGACCATCTCTGGCATTCCAGCCAACCAGCACCGCCTGACCCTC
ACCAGACTTGACCCCGGGAGCTTGTATGAAGTGGAGATGGCAGCTTACAACTGTGCGGGAGAGGGCCAGACAGCC
ATGGTCACCTTCCGAACTGGACGGCGGCCCAAACCCGAGATCATGGCCAGCAAAGAGCAGCAGATCCAGAGAGAC
GACCCTGGAGCCAGTCCCCAGAGCAGCAGCCAGCCAGACCACGGCCGCCTCTCCCCCCCAGAAGCTCCCGACAGG
CCCACCATCTCCACGGCCTCCGAGACCTCAGTGTACGTGACCTGGATTCCCCGTGGGAATGGTGGGTTCCCAATC
CAGTCCTTCCGTGTGGAGTACAAGAAGCTAAAGAAAGTGGGAGACTGGATTCTGGCCACCAGCGCCATCCCCCCA
TCGCGGCTGTCCGTGGAGATCACGGGCCTAGAGAAAGGCACCTCCTACAAGTTTCGAGTCCGGGCTCTGAACATG
CTGGGGGAGAGCGAGCCCAGCGCCCCCTCTCGGCCCTACGTGGTGTCGGGCTACAGCGGTCGCGTGTACGAGAGG
CCCGTGGCAGGTCCTTATATCACCTTCACGGATGCGGTCAATGAGACCACCATCATGCTCAAGTGGATGTACATC
CCAGCAAGTAACAACAACACCCCAATCCATGGCTTTTATATCTATTATCGACCCACAGACAGTGACAATGATAGT
GACTACAAGAAGGATATGGTGGAAGGGGACAAGTACTGGCACTCCATCAGCCACCTGCAGCCAGAGACCTCCTAC
GACATTAAGATGCAGTGCTTCAATGAAGGAGGGGAGAGCGAGTTCAGCAACGTGATGATCTGTGAGACCAAAGCT
CGGAAGTCTTCTGGCCAGCCTGGTCGACTGCCACCCCCAACTCTGGCCCCACCACAGCCGCCCCTTCCTGAAACC
ATAGAGCGGCCGGTGGGCACTGGGGCCATGGTGGCTCGCTCCAGCGACCTGCCCTATCTGATTGTCGGGGTCGTC
CTGGGCTCCATCGTTCTCATCATCGTCACCTTCATCCCCTTCTGCTTGTGGAGGGCCTGGTCTAAGCAAAAACAT
ACAACAGACCTGGGTTTTCCTCGAAGTGCCCTTCCACCCTCCTGCCCGTATACTATGGTGCCATTGGGAGGACTC
CCAGGCCACCAGGCCAGTGGACAGCCCTACCTCAGTGGCATCAGTGGACGGGCCTGTGCTAATGGGATCCACATG
AATAGGGGCTGCCCCTCGGCTGCAGTGGGCTACCCGGGCATGAAGCCCCAGCAGCACTGCCCAGGCGAGCTTCAG
CAGCAGAGTGACACCAGCAGCCTGCTGAGGCAGACCCATCTTGGCAATGGATATGACCCCCAAAGTCACCAGATC
ACGAGGGGTCCCAAGTCTAGCCCGGACGAGGGCTCTTTCTTATACACACTGCCCGACGACTCCACTCACCAGCTG
CTGCAGCCCCATCACGACTGCTGCCAACGCCAGGAGCAGCCTGCTGCTGTGGGCCAGTCAGGGGTGAGGAGAGCC
CCCGACAGTCCTGTCCTGGAAGCAGTGTGGGACCCTCCATTTCACTCAGGGCCCCCATGCTGCTTGGGCCTTGTG
CCAGTTGAAGAGGTGGACAGTCCTGACTCCTGCCAAGTGAGTGGAGGAGACTGGTGTCCCCAGCACCCCGTAGGG
GCCTACGTAGGACAGGAACCTGGAATGCAGCTCTCCCCGGGGCCACTGGTGCGTGTGTCTTTTGAAACACCACCT
CTCACAATT**TAG**GCAGAAGCTGATATCCCAGAAAGACTATATATTGTTTTTTTTTTAAAAAAAAAAAGAAGAAAAA
AGAGACAGAGAAAATTGGTATTTATTTTTCTATTATAGCCATATTTATATATTTATGCACTTGTAAATAAATGTA
TATGTTTTATAATTCTGGAGAGACATAAGGAGTCCTACCCGTTGAGGTTGGAGAGGGAAAATAAAGAAGCTGCCA
CCTAACAGGAGTCACCCAGGAAAGCACCGCACAGGCTGGCGCGGGACAGACTCCTAACCTGGGGCCTCTGCAGTG
GCAGGCGAGGCTGCAGGAGGCCCACAGATAAGCTGGCAAGAGGAAGGATCCCAGGCACATGGTTCATCACGAGCA
TGAGGGAACAGCAAGGGGCACGGTATCACAGCCTGGAGACACCCACACAGATGGCTGGATCCGGTGCTACGGGAA
ACATTTTCCTAAGATGCCCATGAGAACAGACCAAGATGTGTACAGCACTATGAGCATTAAAAAACCTTCCAGAAT
CAATAATCCGTGGCAACATATCTCTGTAAAAACAAACACTGTAACTTCTAAATAAATGTTTAGTCTTCCCTGTAAAA

FIGURE 36

MLRGTMTAWRGMRPEVTLACLLLATAGCFADLNEVPQVTVQPASTVQKPGGTVILGCVVEPP
RMNVTWRLNGKELNGSDDALGVLITHGTLVITALNNHTVGRYQCVARMPAGAVASVPATVTL
ANLQDFKLDVQHVIEVDEGNTAVIACHLPESHPKAQVRYSVKQEWLEASRGNYLIMPSGNLQ
IVNASQEDEGMYKCAAYNPVTQEVKTSGSSDRLRVRRSTAEAARIIYPPEAQTIIVTKGQSL
ILECVASGIPPPRVTWAKDGSSVTGYNKTRFLLSNLLIDTTSEEDSGTYRCMADNGVGQPGA
AVILYNVQVFEPPEVTMELSQLVIPWGQSAKLTCEVRGNPPPSVLWLRNAVPLISSQRLRLS
RRALRVLSMGPEDEGVYQCMAENEVGSAHAVVQLRTSRPSITPRLWQDAELATGTPPVSPSK
LGNPEQMLRGQPALPRPPTSVGPASPKCPGEKGQGAPAEAPIILSSPRTSKTDSYELVWRPR
HEGSGRAPILYYVVKHRKQVTNSSDDWTISGIPANQHRLTLTRLDPGSLYEVEMAAYNCAGE
GQTAMVTFRTGRRPKPEIMASKEQQIQRDDPGASPQSSSQPDHGRLSPPEAPDRPTISTASE
TSVYVTWIPRGNGGFPIQSFRVEYKKLKKVGDWILATSAIPPSRLSVEITGLEKGTSYKFRV
RALNMLGESEPSAPSRPYVVSGYSGRVYERPVAGPYITFTDAVNETTIMLKWMYIPASNNNT
PIHGFYIYYRPTDSDNDSDYKKDMVEGDKYWHSISHLQPETSYDIKMQCFNEGGESEFSNVM
ICETKARKSSGQPGRLPPPTLAPPQPPLPETIERPVGTGAMVARSSDLPYLIVGVVLGSIVL
IIVTFIPFCLWRAWSKQKHTTDLGFPRSALPPSCPYTMVPLGGLPGHQASGQPYLSGISGRA
CANGIHMNRGCPSAAVGYPGMKPQQHCPGELQQQSDTSSLLRQTHLGNGYDPQSHQITRGPK
SSPDEGSFLYTLPDDSTHQLLQPHHDCCQRQEQPAAVGQSGVRRAPDSPVLEAVWDPPFHSG
PPCCLGLVPVEEVDSPDSCQVSGGDWCPQHPVGAYVGQEPGMQLSPGPLVRVSFETPPLTI

Signal peptide:

amino acids 1-30

Transmembrane domain:

amino acids 16-30 (type II), 854-879

FIGURE 37

CGGGAGGCTGGGTCGTCATGATCCGGACCCCATTGTCGGCCTCTGCCCATCGCCTGCTCCTC
CCAGGCTCCCGCGGCCGACCCCCGCGCAAC**ATG**CAGCCCACGGGCCGCGAGGGTTCCCGCGC
GCTCAGCCGGCGGTATCTGCGGCGTCTGCTGCTCCTGCTACTGCTGCTGCTGCTGCGGCAGC
CCGTAACCCGCGCGGAGACCACGCCGGGCGCCCCCAGAGCCCTCTCCACGCTGGGCTCCCCC
AGCCTCTTCACCACGCCGGGTGTCCCCAGCGCCCTCACTACCCCAGGCCTCACTACGCCAGG
CACCCCCAAAACCCTGGACCTTCGGGGTCGCGCGCAGGCCCTGATGCGGAGTTTCCCACTCG
TGGACGGCCACAATGACCTGCCCCAGGTCCTGAGACAGCGTTACAAGAATGTGCTTCAGGAT
GTTAACCTGCGAAATTTCAGCCATGGTCAGACCAGCCTGGACAGGCTTAGAGACGGCCTCGT
GGGTGCCCAGTTCTGGTCAGCCTCCGTCTCATGCCAGTCCCAGGACCAGACTGCCGTGCGCC
TCGCCCTGGAGCAGATTGACCTCATTCACCGCATGTGTGCCTCCTACTCTGAACTCGAGCTT
GTGACCTCAGCTGAAGGTCTGAACAGCTCTCAAAAGCTGGCCTGCCTCATTGGCGTGNAGGG
TGGTCACTCACTGGACAGCAGCCTCTCTGTGCTGCGCAGTTTCTATGTGCTGGGGGTGCGCT
ACCTGACACTTACCTTCACCTGCAGTACACCATGGGCAGAGAGTTCCACCAAGTTCAGACAC
CACATGTACACCAACGTCAGCGGATTGACAAGCTTTGGTGAGAAAGTAGTAGAGGAGTTGAA
CCGCCTGGGCATGATGATAGATTTGTCCTATGCATCGGACACCTTGATAAGAAGGGTCCTGG
AAGTGTCTCAGGCTCCTGTGATCTTCTCCCACTCAGCTGCCAGAGCTGTGTGTGACAATTTG
TTGAATGTTCCCGATGATATCCTGCAGCTTCTGAAGAACGGTGGCATCGTGATGGTGACACT
GTCCATGGGGGTGCTGCAGTGCAACCTGCTTGCTAACGTGTCCACTGTGGCAGATCACTTTG
ACCACATCAGGGCAGTCATTGGATCTGAGTTCATCGGGATTGGTGGAAATTATGACGGGACT
GGCCGGTTCCCTCAGGGGCTGGAGGATGTGTCCACATACCCAGTCCTGATAGAGGAGTTGCT
GAGTCGTASCTGGAGCGAGGAAGAGCTTCAAGGTGTCCTTCGTGGAAACCTGCTGCGGGTCT
TCAGACAAGTGGAAAAGGTGAGAGAGGAGAGCAGGGCGCAGAGCCCCGTGGAGGCTGAGTTT
CCATATGGGCAACTGAGCACATCCTGCCACTCCCACCTCGTGCCTCAGAATGGACACCAGGC
TACTCATCTGGAGGTGACCAAGCAGCCAACCAATCGGGTCCCCTGGAGGTCCTCAAATGCCT
CCCCATACCTTGTTCCAGGCCTTGTGGCTGCTGCCACCATCCCAACCTTCACCCAGTGGCTC
TGC**TGA**CACAGTCGGTCCCCGCAGAGGTCACTGTGGCAAAGCCTCACAAAGCCCCCTCTCCT
AGTTCATTCACAAGCATATGCTGAGAATAAACATGTTACACATGGAAAA

FIGURE 38

><usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59817
><subunit 1 of 1, 487 aa, 1 stop, 2 unknown
><MW: 53569.32, pI: 7.68, NX(S/T): 5
MQPTGREGSRALSRRYLRRLLLLLLLLLLRQPVTRAETTPGAPRALSTLGSPSLFTTPGVPS
ALTTPGLTTPGTPKTLDLRGRAQALMRSFPLVDGHNDLPQVLRQRYKNVLQDVNLRNFSHGQ
TSLDRLRDGLVGAQFWSASVSCQSQDQTAVRLALEQIDLIHRMCASYSELELVTSAEGLNSS
QKLACLIGVXGGHSLDSSLSVLRSFYVLGVRYLTLTFTCSTPWAESSTKFRHHMYTNVSGLT
SFGEKVVEELNRLGMMIDLSYASDTLIRRVLEVSQAPVIFSHSAARAVCDNLLNVPDDILQL
LKNGGIVMVTLSMGVLQCNLLANVSTVADHFDHIRAVIGSEFIGIGGNYDGTGRFPQGLEDV
STYPVLIEELLSRXWSEEELQGVLRGNLLRVFRQVEKVREESRAQSPVEAEFPYGQLSTSCH
SHLVPQNGHQATHLEVTKQPTNRVPWRSSNASPYLVPGLVAAATIPTFTQWLC

Important features of the protein:

Signal peptide:
amino acids 1-36

Transmembrane domain:
amino acids 313-331

N-glycosylation sites.
amino acids 119-122, 184-187, 243-246 and 333-336

N-myristoylation sites.
amino acids 41-46, 59-64, 73-78, 133-138, 182-187, 194-199, 324-329, 354-359, 357-362, 394-399, 427-432 and 472-477.

Prokaryotic membrane lipoprotein lipid attachment site.
amino acids 136-146

FIGURE 39

TGCTAGGCTCTGTCCCACAATGCACCCGAGAGCAGGAGCTGAAAGCCTCTAACACCCACAGA
TCCCTCTATGACTGCAATGTGAGGTGTCCGGCTTTGCTGGCCCAGCAAGCCTGATAAGC**ATG**
AAGCTCTTATCTTTGGTGGCTGTGGTCGGGTGTTTGCTGGTGCCCCCAGCTGAAGCCAACAA
GAGTTCTGAAGATATCCGGTGCAAATGCATCTGTCCACCTTATAGAAACATCAGTGGGCACA
TTTACAACCAGAATGTATCCCAGAAGGACTGCAACTGCCTGCACGTGGTGGAGCCCATGCCA
GTGCCTGGCCATGACGTGGAGGCCTACTGCCTGCTGTGCGAGTGCAGGTACGAGGAGCGCAG
CACCACCACCATCAAGGTCATCATTGTCATCTACCTGTCCGTGGTGGGTGCCCTGTTGCTCT
ACATGGCCTTCCTGATGCTGGTGGACCCTCTGATCCGAAAGCCGGATGCATACACTGAGCAA
CTGCACAATGAGGAGGAGAATGAGGATGCTCGCTCTATGGCAGCAGCTGCTGCATCCCTCGG
GGGACCCCGAGCAAACACAGTCCTGGAGCGTGTGGAAGGTGCCCAGCAGCGGTGGAAGCTGC
AGGTGCAGGAGCAGCGGAAGACAGTCTTCGATCGGCACAAGATGCTCAGC**TAG**ATGGGCTGG
TGTGGTTGGGTCAAGGCCCCAACACCATGGCTGCCAGCTTCCAGGCTGGACAAAGCAGGGGG
CTACTTCTCCCTTCCCTCGGTTCCAGTCTTCCCTTTAAAAGCCTGTGGCATTTTTCCTCCTT
CTCCCTAACTTTAGAAATGTTGTACTTGGCTATTTTGATTAGGGAAGAGGGATGTGGTCTCT
GATCTCTGTTGTCTTCTTGGGTCTTTGGGGTTGAAGGGAGGGGGAAGGCAGGCCAGAAGGGA
ATGGAGACATTCGAGGCGGCCTCAGGAGTGGATGCGATCTGTCTCTCCTGGCTCCACTCTTG
CCGCCTTCCAGCTCTGAGTCTTGGGAATGTTGTTACCCTTGGAAGATAAAGCTGGGTCTTCA
GGAACTCAGTGTCTGGGAGGAAAGCATGGCCCAGCATTCAGCATGTGTTCCTTTCTGCAGTG
GTTCTTATCACCACCTCCCTCCCAGCCCCGGCGCCTCAGCCCCAGCCCCAGCTCCAGCCCTG
AGGACAGCTCTGATGGGAGAGCTGGGCCCCCTGAGCCCACTGGGTCTTCAGGGTGCACTGGA
AGCTGGTGTTCGCTGTCCCCTGTGCACTTCTCGCACTGGGGCATGGAGTGCCCATGCATACT
CTGCTGCCGGTCCCCTCACCTGCACTTGAGGGGTCTGGGCAGTCCCTCCTCTCCCCAGTGTC
CACAGTCACTGAGCCAGACGGTCGGTTGGAACATGAGACTCGAGGCTGAGCGTGGATCTGAA
CACCACAGCCCCTGTACTTGGGTTGCCTCTTGTCCCTGAACTTCGTTGTACCAGTGCATGGA
GAGAAAATTTTGTCCTCTTGTCTTAGAGTTGTGTGTAAATCAAGGAAGCCATCATTAAATTG
TTTTATTTCTCTCA

FIGURE 40

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA60278

<subunit 1 of 1, 183 aa, 1 stop

<MW: 20574, pI: 6.60, NX(S/T): 3

MKLLSLVAVVGCLLVPPAEANKSSEDIRCKCICPPYRNISGHIYNQNVSQKDCNCLHVVEPM
PVPGHDVEAYCLLCECRYEERSTTTIKVIIVIYLSVVGALLLYMAFLMLVDPLIRKPDAYTE
QLHNEEENEDARSMAAAAASLGGPRANTVLERVEGAQQRWKLQVQEQRKTVFDRHKMLS

Important features:

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 90-112

N-glycosylation sites.

amino acids 21-24, 38-41 and 47-50

FIGURE 41

AGCGGGTCTCGCTTGGGTTCCGCTAATTTCTGTCCTGAGGCGTGAGACTGAGTTCATAGGGTCCTGGGTCCCCGA
ACCAGGAAGGGTTGAGGGAACACAATCTGCAAGCCCCCGCGACCCAAGTGAGGGGCCCCGTGTTGGGGTCCTCCC
TCCCTTTGCATTCCCACCCCTCCGGGCTTTGCGTCTTCCTGGGGACCCCCTCGCCGGGAG**ATG**GCCGCGTTGATG
CGGAGCAAGGATTCGTCCTGCTGCCTGCTCCTACTGGCCGCGGTGCTGATGGTGGAGAGCTCACAGATCGGCAGT
TCGCGGGCCAAACTCAACTCCATCAAGTCCTCTCTGGGCGGGGAGACGCCTGGTCAGGCCGCCAATCGATCTGCG
GGCATGTACCAAGGACTGGCATTCGGCGGCAGTAAGAAGGGCAAAAACCTGGGGCAGGCCTACCCTTGTAGCAGT
GATAAGGAGTGTGAAGTTGGGAGGTATTGCCACAGTCCCCACCAAGGATCATCGGCCTGCATGGTGTGTCGGAGA
AAAAAGAAGCGCTGCCACCGAGATGGCATGTGCTGCCCCAGTACCCGCTGCAATAATGGCATCTGTATCCCAGTT
ACTGAAAGCATCTTAACCCCTCACATCCCGGCTCTGGATGGTACTCGGCACAGAGATCGAAACCACGGTCATTAC
TCAAACCATGACTTGGGATGGCAGAATCTAGGAAGACCACACACTAAGATGTCACATATAAAAGGGCATGAAGGA
GACCCCTGCCTACGATCATCAGACTGCATTGAAGGGTTTTGCTGTGCTCGTCATTTCTGGACCAAAATCTGCAAA
CCAGTGCTCCATCAGGGGGAAGTCTGTACCAAACAACGCAAGAAGGGTTCTCATGGGCTGGAAATTTTCCAGCGT
TGCGACTGTGCGAAGGGCCTGTCTTGCAAAGTATGGAAAGATGCCACCTACTCCTCCAAAGCCAGACTCCATGTG
TGTCAGAAAATT**TGA**TCACCATTGAGGAACATCATCAATTGCAGACTGTGAAGTTGTGTATTTAATGCATTATAG
CATGGTGGAAAATAAGGTTCAGATGCAGAAGAATGGCTAAAATAAGAAACGTGATAAGAATATAGATGATCACAA
AAAGGGAGAAAGAAAACATGAACTGAATAGATTAGAATGGGTGACAAATGCAGTGCAGCCAGTGTTTCCATTATG
CAACTTGTCTATGTAAATAATGTACACATTTGTGGAAAATGCTATTATTAAGAGAACAAGCACACAGTGGAAATT
ACTGATGAGTAGCATGTGACTTTCCAAGAGTTTAGGTTGTGCTGGAGGAGAGGTTTCCTTCAGATTGCTGATTGC
TTATACAAATAACCTACATGCCAGATTTCTATTCAACGTTAGAGTTTAACAAAATACTCCTAGAATAACTTGTTA
TACAATAGGTTCTAAAAATAAAATTGCTAAACAAGAAATGAAAACATGGAGCATTGTTAATTTACAACAGAAAAT
TACCTTTTGATTTGTAACACTACTTCTGCTGTTCAATCAAGAGTCTTGGTAGATAAGAAAAAAATCAGTCAATAT
TTCCAAATAATTGCAAAATAATGGCCAGTTGTTTAGGAAGGCCTTTAGGAAGACAAATAAATAACAAACAAACAG
CCACAAATACTTTTTTTTTCAAAATTTTAGTTTTACCTGTAATTAATAAGAACTGATACAAGACAAAAACAGTTCC
TTCAGATTCTACGGAATGACAGTATATCTCTCTTTATCCTATGTGATTCCTGCTCTGAATGCATTATATTTTCCA
AACTATACCCATAAATTGTGACTAGTAAAATACTTACACAGAGCAGAATTTTCACAGATGGCAAAAAAATTTAAA
GATGTCCAATATATGTGGGAAAAGAGCTAACAGAGAGATCATTATTTCTTAAAGATTGGCCATAACCTATATTTT
GATAGAATTAGATTGGTAAATACATGTATTCATACATACTCTGTGGTAATAGAGACTTAAGCTGGATCTGTACTG
CACTGGAGTAAGCAAGAAAATTGGGAAAACTTTTTCGTTTGTTCAGGTTTTGGCAACACATAGATCATATGTCTG
AGGCACAAGTTGGCTGTTCATCTTTGAAACCAGGGGATGCACAGTCTAAATGAATATCTGCATGGGATTTGCTAT
CATAATATTTACTATGCAGATGAATTCAGTGTGAGGTCCTGTGTCCGTACTATCCTCAAATTATTTATTTTATAG
TGCTGAGATCCTCAAATAATCTCAATTTCAGGAGGTTTCACAAAATGTACTCCTGAAGTAGACAGAGTAGTGAGG
TTTCATTGCCCTCTATAAGCTTCTGACTAGCCAATGGCATCATCCAATTTTCTTCCCAAACCTCTGCAGCATCTG
CTTTATTGCCAAAGGGCTAGTTTCGGTTTTCTGCAGCCATTGCGGTTAAAAAATATAAGTAGGATAACTTGTAAA
ACCTGCATATTGCTAATCTATAGACACCACAGTTTCTAAATTCTTTGAAACCACTTTACTACTTTTTTTAAACTT
AACTCAGTTCTAAATACTTTGTCTGGAGCACAAAACAATAAAAGGTTATCTTATAGTCGTGACTTTAAACTTTTG
TAGACCACAATTCACTTTTTAGTTTTCTTTTACTTAAATCCCATCTGCAGTCTCAAATTTAAGTTCTCCCAGTAG
AGATTGAGTTTGAGCCTGTATATCTATTAAAAATTTCAACTTCCCACATATATTTACTAAGATGATTAAGACTTA
CATTTTCTGCACAGGTCTGCAAAAACAAAAATTATAAACTAGTCCATCCAAGAACCAAAGTTTGTATAAACAGGT
TGCTATAAGCTTGTGAAATGAAAATGGAACATTTCAATCAAACATTTCCTATATAACAATTATTATATTTACAAT
TTGGTTTCTGCAATATTTTTCTTATGTCCACCCTTTTAAAAATTATTATTTGAAGTAATTTATTTACAGGAAATG
TTAATGAGATGTATTTTCTTATAGAGATATTTCTTACAGAAAGCTTTGTAGCAGAATATATTTGCAGCTATTGAC
TTTGTAATTTAGGAAAAATGTATAATAAGATAAAATCTATTAAATTTTTCTCCTCTAAAAACTGAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAA

FIGURE 42

MAALMRSKDSSCCLLLLAAVLMVESSQIGSSRAKLNSIKSSLGGETPGQAANRSAGMYQGLA
FGGSKKGKNLGQAYPCSSDKECEVGRYCHSPHQGSSACMVCRRKKKRCHRDGMCCPSTRCNN
GICIPVTESILTPHIPALDGTRHRDRNHGHYSNHDLGWQNLGRPHTKMSHIKGHEGDPCLRS
SDCIEGFCCARHFWTKICKPVLHQGEVCTKQRKKGSHGLEIFQRCDCAKGLSCKVWKDATYS
SKARLHVCQKI

Signal peptide:

amino acids 1-25

FIGURE 43

TCTCAATCTGCTGACCTCGTGATCCGCCTGACCTTGTAATCCACCTACCTTGGCCTCCCAAA
GTGTTGGGATTACAGGCGTGAGCCACCGCGCCCGGCCAACATCACGTTTTTAAAAATTGATT
TCTTCAAATTCATGGCAAATATTTCCCTTCCCTTTAACTTCTTATGTCAGAATGAGGAAGGA
TAGCTGCATTTATTTAGTCAGTTTTCATTGCATAGTAATATTTTCATGTAGTATTTTCTAAG
TTATATTTTAGTAATTCATATGTTTTAGATTATAGGTTTTAACATACTTGTGAAAATACTTG
ATGTGTTTTAAAGCCTTGGGCAGAAATTCTGTATTGTTGAGGATTTGTTCTTTTATCCCCCT
TTTAAAGTCATCCGTCCTTGGCTCAGGATTTGGAGAGCTTGCACCACCAAAAATGGCAAACA
TCACCAGCTCCCAGATTTTGGACCAGTTGAAAGCTCCGAGTTTGGGCCAGTTTACCACCACC
CCAAGTACACAGCAGAATAGTACAAGTCACCCTACAACTACTACTTCTTGGGACCTCAAGCC
CCCAACATCCCAGTCCTCAGTCCTCAGTCATCTTGACTTCAAATCTCAACCTGAGCCATCCC
CAGTTCTTAGCCAGTTGAGCCAGCGACAACAGCACCAGAGCCAGGCAGTCACTGTTCCTCCT
CCTGGTTTGGAGTCCTTTCCTTCCCAGGCAAAACTTCGAGAATCAACACCTGGAGACAGTCC
CTCCACTGTGAACAAGCTTTTGCAGCTTCCCAGCACGACCATTGAAAATATCTCTGTGTCTG
TCCACCAGCCACAGCCCAAACACATCAAACTTGCTAAGCGGCGGATACCCCCAGCTTCTAAG
ATCCCAGCTTCTGCAGTGGAAATGCCTGGTTCAGCAGATGTCACAGGATTAAATGTGCAGTT
TGGGGCTCTGGAATTTGGGTCAGAACCTTCTCTCTCTGAATTTGGATCAGCTCCAAGCAGTG
AAAATAGTAATCAGATTCCCATCAGCTTGTATTCGAAGTCTTTAAGTGAGCCTTTGAATACA
TCTTTATCAATGACCAGTGCAGTACAGAACTCCACATATACAACTTCCGTCATTACCTCCTG
CAGTCTGACAAGCTCATCACTGAATTCTGCTAGTCCAGTAGCAATGTCTTCCTCTTATGACC
AGAGTTCTGTGCATAACAGGATCCCATACCAAAGCCCTGTGAGTTCATCAGAGTCAGCTCCA
GGAACCATCATGAATGGACATGGTGGTGGTCGAAGTCAGCAGACACTAGACAGTAAGTATAG
CAGCAAGCTACTCTTGTCATGGCTGGTGCCAACCAAACAGAGGAAGAGGATAGCTCACGTGA
TGTGGAAAACACCAGTTGGTCAATGGCTCATTCGT**TAA**AAAGCAGCCCTTTTGCTTTTTTGT
TTTTGGACCAGGTGTTGGCTGTGGTGTTATTAGAAATGTCTTAACCACAGCAAGAAGGAGGT
GGTGGTCTCATATTCTTCTGCCCTAATCAGACTGCACCACAAGTGCAGCATACAGTATGCAT
TTTAAAGATGCTTGGGCCAGGCGGGGTGGCTGATGCCCATAATCCCAGTGCTTTGGGGGGCC
AAGGCAGGCAGATTGCCCAAGCTCAGGAGTTTGAGACCACCCTGGGCAACATGGTGAAACTC
TGTCTCTACTAAAATACGAAAAACTAGCCGGGTGTGGTGGCGGCGCGTGCCTGTAATCCCAG
CTACTTGGGAGGCTGAGGCACAAGAATCGCTTGAGCCAGCTTGGGCTACAAAGTGAGACTCC
GTCTGAAAAGA

FIGURE 44

MCFKALGRNSVLLRICSFIPLLKSSVLGSGFGELAPPKMANITSSQILDQLKAPSLGQFTTT
PSTQQNSTSHPTTTTSWDLKPPTSQSSVLSHLDFKSQPEPSPVLSQLSQRQQHQSQAVTVPP
PGLESFPSQAKLRESTPGDSPSTVNKLLQLPSTTIENISVSVHQPQPKHIKLAKRRIPPASK
IPASAVEMPGSADVTGLNVQFGALEFGSEPSLSEFGSAPSSENSNQIPISLYSKSLSEPLNT
SLSMTSAVQNSTYTTSVITSCSLTSSSLNSASPVAMSSSYDQSSVHNRIPYQSPVSSSESAP
GTIMNGHGGGRSQQTLDSKYSSKLLLSWLVPTKQRKRIAHVMWKTPVGQWLIR

Signal peptide:

amino acids 1-24

FIGURE 45

GCCGAGTGGGACAAAGCCTGGGGCTGGGCGGGGGCC**ATG**GCGCTGCCATCCCGAATCCTGCT
TTGGAAACTTGTGCTTCTGCAGAGCTCTGCTGTTCTCCTGCACTCAGCGGTGGAGGAGACGG
ACGCGGGGCTGTACACCTGCAACCTGCACCATCACTACTGCCACCTCTACGAGAGCCTGGCC
GTCCGCCTGGAGGTCACCGACGGCCCCCCGGCCACCCCCGCCTACTGGGACGGCGAGAAGGA
GGTGCTGGCGGTGGCGCGCGGCGCACCCGCGCTTCTGACCTGCGTGAACCGCGGGCACGTGT
GGACCGACCGGCACGTGGAGGAGGCTCAACAGGTGGTGCACTGGGACCGGCAGCCGCCCGGG
GTCCCGCACGACCGCGCGGACCGCCTGCTGGACCTCTACGCGTCGGGCGAGCGCCGCGCCTA
CGGGCCCCTTTTTCTGCGCGACCGCGTGGCTGTGGGCGCGGATGCCTTTGAGCGCGGTGACT
TCTCACTGCGTATCGAGCCGCTGGAGGTCGCCGACGAGGGCACCTACTCCTGCCACCTGCAC
CACCATTACTGTGGCCTGCACGAACGCCGCGTCTTCCACCTGACGGTCGCCGAACCCCACGC
GGAGCCGCCCCCCCGGGGCTCTCCGGGCAACGGCTCCAGCCACAGCGGCGCCCCAGGCCCAG
ACCCCACACTGGCGCGCGGCCACAACGTCATCAATGTCATCGTCCCCGAGAGCCGAGCCCAC
TTCTTCCAGCAGCTGGGCTACGTGCTGGCCACGCTGCTGCTCTTCATCCTGCTACTGGTCAC
TGTCCTCCTGGCCGCCCGCAGGCGCCGCGGAGGCTACGAATACTCGGACCAGAAGTCGGGAA
AGTCAAAGGGGAAGGATGTTAACTTGGCGGAGTTCGCTGTGGCTGCAGGGGACCAGATGCTT
TACAGGAGTGAGGACATCCAGCTAGATTACAAAAACAACATCCTGAAGGAGAGGGCGGAGCT
GGCCCACAGCCCCCTGCCTGCCAAGTACATCGACCTAGACAAAGGGTTCCGGAAGGAGAACT
GCAAA**TAG**GGAGGCCCTGGGCTCCTGGCTGGGCCAGCAGCTGCACCTCTCCTGTCTGTGCTC
CTCGGGGCATCTCCTGATGCTCCGGGGCTCACCCCCCTTCCAGCGGCTGGTCCCGCTTTCCT
GGAATTTGGCCTGGGCGTATGCAGAGGCCGCCTCCACACCCCTCCCCCAGGGGCTTGGTGGC
AGCATAGCCCCCACCCCTGCGGCCTTTGCTCACGGGTGGCCCTGCCCACCCCTGGCACAACC
AAAATCCCACTGATGCCCATCATGCCCTCAGACCCTTCTGGGCTCTGCCCGCTGGGGGCCTG
AAGACATTCCTGGAGGACACTCCCATCAGAACCTGGCAGCCCCAAAACTGGGGTCAGCCTCA
GGGCAGGAGTCCCACTCCTCCAGGGCTCTGCTCGTCCGGGGCTGGGAGATGTTCCTGGAGGA
GGACACTCCCATCAGAACTTGGCAGCCTTGAAGTTGGGGTCAGCCTCGGCAGGAGTCCCACT
CCTCCTGGGGTGCTGCCTGCCACCAAGAGCTCCCCCACCTGTACCACCATGTGGGACTCCAG
GCACCATCTGTTCTCCCCAGGGACCTGCTGACTTGAATGCCAGCCCTTGCTCCTCTGTGTTG
CTTTGGGCCACCTGGGGCTGCACCCCCTGCCCTTTCTCTGCCCCATCCCTACCCTAGCCTTG
CTCTCAGCCACCTTGATAGTCACTGGGCTCCCTGTGACTTCTGACCCTGACACCCCTCCCTT
GGACTCTGCCTGGGCTGGAGTCTAGGGCTGGGGCTACATTTGGCTTCTGTACTGGCTGAGGA
CAGGGGAGGGAGTGAAGTTGGTTTGGGGTGGCCTGTGTTGCCACTCTCAGCACCCCACATTT
GCATCTGCTGGTGGACCTGCCACCATCACAATAAAGTCCCCATCTGATTTTAAAAAAAAAA
AAAAA

FIGURE 46

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA60618
<subunit 1 of 1, 341 aa, 1 stop
<MW: 38070, pI: 6.88, NX(S/T): 1
MALPSRILLWKLVLLQSSAVLLHSAVEETDAGLYTCNLHHHYCHLYESLAVRLEVTDGPPAT
PAYWDGEKEVLAVARGAPALLTCVNRGHVWTDRHVEEAQQVVHWDRQPPGVPHDRADRLLDL
YASGERRAYGPLFLRDRVAVGADAFERGDFSLRIEPLEVADEGTYSCHLHHHYCGLHERRVF
HLTVAEPHAEPPPRGSPGNGSSHSGAPGPDPTLARGHNVINVIVPESRAHFFQQLGYVLATL
LLFILLLVTVLLAARRRRGGYEYSDQKSGKSKGKDVNLAEFAVAAGDQMLYRSEDIQLDYKN
NILKERAELAHSPLPAKYIDLDKGFRKENCK

Important features:

Signal peptide:
amino acids 1-19

Transmembrane domain:
amino acids 237-262

N-glycosylation site.
amino acids 205-208

Cell attachment sequence.
amino acids 151-154

Coproporphyrinogen III oxidase proteins.
amino acids 115-140

FIGURE 47

CGCCGGAGGCAGCGGCGGCGTGGCGCAGCGGCGAC**ATG**GCCGTTGTCTCAGAGGACGACTTT
CAGCACAGTTCAAACTCCACCTACGGAACCACAAGCAGCAGTCTCCGAGCTGACCAGGAGGC
ACTGCTTGAGAAGCTGCTGGACCGCCCGCCCCCTGGCCTGCAGAGGCCCGAGGACCGCTTCT
GTGGCACATACATCATCTTCTTCAGCCTGGGCATTGGCAGTCTACTGCCATGGAACTTCTTT
ATCACTGCCAAGGAGTACTGGATGTTCAAACTCCGCAACTCCTCCAGCCCAGCCACCGGGGA
GGACCCTGAGGGCTCAGACATCCTGAACTACTTTGAGAGCTACCTTGCCGTTGCCTCCACCG
TGCCCTCCATGCTGTGCCTGGTGGCCAACTTCCTGCTTGTCAACAGGGTTGCAGTCCACATC
CGTGTCCTGGCCTCACTGACGGTCATCCTGGCCATCTTCATGGTGATAACTGCACTGGTGAA
GGTGGACACTTCCTCCTGGACCCGTGGTTTTTTGCGGTCACCATTGTCTGCATGGTGATCC
TCAGCGGTGCCTCCACTGTCTTCAGCAGCAGCATCTACGGCATGACCGGCTCCTTTCCTATG
AGGAACTCCCAAGCACTGATATCAGGAGGAGCCATGGGCGGGACGGTCAGCGCCGTGGCCTC
ATTGGTGGACTTGGCTGCATCCAGTGATGTGAGGAACAGCGCCCTGGCCTTCTTCCTGACGG
CCACCATCTTCCTCGTGCTCTGCATGGGACTCTACCTGCTGCTGTCCAGGCTGGAGTATGCC
AGGTACTACATGAGGCCTGTTCTTGCGGCCCATGTGTTTTCTGGTGAAGAGGAGCTTCCCCA
GGACTCCCTCAGTGCCCCTTCGGTGGCCTCCAGATTCATTGATTCCCACACACCCCCTCTCC
GCCCCATCCTGAAGAAGACGGCCAGCCTGGGCTTCTGTGTCACCTACGTCTTCTTCATCACC
AGCCTCATCTACCCCGCCGTCTGCACCAACATCGAGTCCCTCAACAAGGGCTCGGGCTCACT
GTGGACCACCAAGTTTTTCATCCCCCTCACTACCTTCCTCCTGTACAACTTTGCTGACCTAT
GTGGCCGGCAGCTCACCGCCTGGATCCAGGTGCCAGGGCCCAACAGCAAGGCGCTCCCAGGG
TTCGTGCTCCTCCGGACCTGCCTCATCCCCCTCTTCGTGCTCTGTAACTACCAGCCCCGCGT
CCACCTGAAGACTGTGGTCTTCCAGTCCGATGTGTACCCCGCACTCCTCAGCTCCCTGCTGG
GGCTCAGCAACGGCTACCTCAGCACCCTGGCCCTCCTCTACGGGCCTAAGATTGTGCCCAGG
GAGCTGGCTGAGGCCACGGGAGTGGTGATGTCCTTTTATGTGTGCTTGGGCTTAACACTGGG
CTCAGCCTGCTCTACCCTCCTGGTGCACCTCATC**TAG**AAGGGAGGACACAAGGACATTGGTG
CTTCAGAGCCTTTGAAGATGAGAAGAGAGTGCAGGAGGGCTGGGGGCCATGGAGGAAAGGCC
TAAAGTTTCACTTGGGGACAGAGAGCAGAGCACACTCGGGCCTCATCCCTCCCAAGATGCCA
GTGAGCCACGTCCATGCCCATTCCGTGCAAGGCAGATATTCCAGTCATATTAACAGAACACT
CCTGAGACAGTTGAAGAAGAAATAGCACAAATCAGGGGTACTCCCTTCACAGCTGATGGTTA
ACATTCCACCTTCTTTCTAGCCCTTCAAAGATGCTGCCAGTGTTCGCCCTAGAGTTATTACA
AAGCCAGTGCCAAAACCCAGCCATGGGCTCTTTGCAACCTCCCAGCTGCGCTCATTCCAGCT
GACAGCGAGATGCAAGCAAATGCTCAGCTCTCCTTACCCTGAAGGGGTCTCCCTGGAATGGA
AGTCCCCTGGCATGGTCAGTCCTCAGGCCCAAGACTCAAGTGTGCACAGACCCCTGTGTTCT
GCGGGTGAACAACTGCCCACTAACCAGACTGGAAAACCCAGAAAGATGGGCCTTCCATGAAT
GCTTCATTCCAGAGGGACCAGAGGGCCTCCCTGTGCAAGGGATCAAGCATGTCTGGCCTGGG
TTTTCAAAAAAAGAGGGATCCTCATGACCTGGTGGTCTATGGCCTGGGTCAAGATGAGGGTC
TTTCAGTGTTCCTGTTTACAACATGTCAAAGCCATTGGTTCAAGGGCGTAATAAATACTTGC
GTATTCAAAAA

FIGURE 48

MAVVSEDDFQHSSNSTYGTTSSSLRADQEALLEKLLDRPPPGLQRPEDRFCGTYIIFFSLGI
GSLLPWNFFITAKEYWMFKLRNSSSPATGEDPEGSDILNYFESYLAVASTVPSMLCLVANFL
LVNRVAVHIRVLASLTVILAIFMVITALVKVDTSSWTRGFFAVTIVCMVILSGASTVFSSSI
YGMTGSFPMRNSQALISGGAMGGTVSAVASLVDLAASSDVRNSALAFFLTATIFLVLCMGLY
LLLSRLEYARYYMRPVLAAHVFSGEEELPQDSLSAPSVASRFIDSHTPPLRPILKKTASLGF
CVTYVFFITSLIYPAVCTNIESLNKGSGSLWTTKFFIPLTTFLLYNFADLCGRQLTAWIQVP
GPNSKALPGFVLLRTCLIPLFVLCNYQPRVHLKTVVFQSDVYPALLSSLLGLSNGYLSTLAL
LYGPKIVPRELAEATGVVMSFYVCLGLTLGSACSTLLVHLI

Transmembrane domain:

amino acids 50-74 (type II), 105-127, 135-153, 163-183, 228-252, 305-330, 448-472

FIGURE 49

GACAGTGGAGGGCAGTGGAGAGGACCGCGCTGTCCTGCTGTCACCAAGAGCTGGAGACACCA

TCTCCCACCGAGAGTC**ATG**GCCCCATTGGCCCTGCACCTCCTCGTCCTCGTCCCCATCCTCC

TCAGCCTGGTGGCCTCCCAGGACTGGAAGGCTGAACGCAGCCAAGACCCCTTCGAGAAATGC

ATGCAGGATCCTGACTATGAGCAGCTGCTCAAGGTGGTGACCTGGGGGCTCAATCGGACCCT

GAAGCCCCAGAGGGTGATTGTGGTTGGCGCTGGTGTGGCCGGGCTGGTGGCCGCCAAGGTGC

TCAGCGATGCTGGACACAAGGTCACCATCCTGGAGGCAGATAACAGGATCGGGGGCCGCATC

TTCACCTACCGGGACCAGAACACGGGCTGGATTGGGGAGCTGGGAGCCATGCGCATGCCCAG

CTCTCACAGGATCCTCCACAAGCTCTGCCAGGGCCTGGGGCTCAACCTGACCAAGTTCACCC

AGTACGACAAGAACACGTGGACGGAGGTGCACGAAGTGAAGCTGCGCAACTATGTGGTGGAG

AAGGTGCCCGAGAAGCTGGGCTACGCCTTGCGTCCCCAGGAAAAGGGCCACTCGCCCGAAGA

CATCTACCAGATGGCTCTCAACCAGGCCCTCAAAGACCTCAAGGCACTGGGCTGCAGAAAGG

CGATGAAGAAGTTTGAAAGGCACACGCTCTTGGAATATCTTCTCGGGGAGGGGAACCTGAGC

CGGCCGGCCGTGCAGCTTCTGGGAGACGTGATGTCCGAGGATGGCTTCTTCTATCTCAGCTT

CGCCGAGGCCCTCCGGGCCCACAGCTGCCTCAGCGACAGACTCCAGTACAGCCGCATCGTGG

GTGGCTGGGACCTGCTGCCGCGCGCGCTGCTGAGCTCGCTGTCCGGGCTTGTGCTGTTGAAC

GCGCCCGTGGTGGCGATGACCCAGGGACCGCACGATGTGCACGTGCAGATCGAGACCTCTCC

CCCGGCGCGGAATCTGAAGGTGCTGAAGGCCGACGTGGTGCTGCTGACGGCGAGCGGACCGG

CGGTGAAGCGCATCACCTTCTCGCCGCCGCTGCCCCGCCACATGCAGGAGGCGCTGCGGAGG

CTGCACTACGTGCCGGCCACCAAGGTGTTCCTAAGCTTCCGCAGGCCCTTCTGGCGCGAGGA

GCACATTGAAGGCGGCCACTCAAACACCGATCGCCCGTCGCGCATGATTTTCTACCCGCCGC

CGCGCGAGGGCGCGCTGCTGCTGGCCTCGTACACGTGGTCGGACGCGGCGGCAGCGTTCGCC

GGCTTGAGCCGGGAAGAGGCGTTGCGCTTGGCGCTCGACGACGTGGCGGCATTGCACGGGCC

TGTCGTGCGCCAGCTCTGGGACGGCACCGGCGTCGTCAAGCGTTGGGCGGAGGACCAGCACA

GCCAGGGTGGCTTTGTGGTACAGCCGCCGGCGCTCTGGCAAACCGAAAAGGATGACTGGACG

GTCCCTTATGGCCGCATCTACTTTGCCGGCGAGCACACCGCCTACCCGCACGGCTGGGTGGA

GACGGCGGTCAAGTCGGCGCTGCGCGCCGCCATCAAGATCAACAGCCGGAAGGGGCCTGCAT

CGGACACGGCCAGCCCCGAGGGGCACGCATCTGACATGGAGGGGCAGGGGCATGTGCATGGG

GTGGCCAGCAGCCCCTCGCATGACCTGGCAAAGGAAGAAGGCAGCCACCCTCCAGTCCAAGG

CCAGTTATCTCTCCAAAACACGACCCACACGAGGACCTCGCAT**TAA**AGTATTTTCGGAAAAA

AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 50

MAPLALHLLVLVPILLSLVASQDWKAERSQDPFEKCMQDPDYEQLLKVVTWGLNRTLKPQRV
IVVGAGVAGLVAAKVLSDAGHKVTILEADNRIGGRIFTYRDQNTGWIGELGAMRMPSSHRIL
HKLCQGLGLNLTKFTQYDKNTWTEVHEVKLRNYVVEKVPEKLGYALRPQEKGHSPEDIYQMA
LNQALKDLKALGCRKAMKKFERHTLLEYLLGEGNLSRPAVQLLGDVMSEDGFFYLSFAEALR
AHSCLSDRLQYSRIVGGWDLLPRALLSSLSGLVLLNAPVVAMTQGPHDVHVQIETSPPARNL
KVLKADVVLLTASGPAVKRITFSPPLPRHMQEALRRLHYVPATKVFLSFRRPFWREEHIEGG
HSNTDRPSRMIFYPPPREGALLLASYTWSDAAAAFAGLSREEALRLALDDVAALHGPVVRQL
WDGTGVVKRWAEDQHSQGGFVVQPPALWQTEKDDWTVPYGRIYFAGEHTAYPHGWVETAVKS
ALRAAIKINSRKGPASDTASPEGHASDMEGQGHVHGVASSPSHDLAKEEGSHPPVQGQLSLQ
NTTHTRTSH

Signal peptide:

amino acids 1-21

FIGURE 51

CTGACATGGCCTGACTCGGGACAGCTCAGAGCAGGGCAGAACTGGGGACACTCTGGGCCGGCCTTCTGCCTGCATG
GACGCTCTGAAGCCACCCTGTCTCTGGAGGAACCACGAGCGAGGGAAGAAGGACAGGGACTCGTGTGGCAGGAA
GAACTCAGAGCCGGGAAGCCCCCATTCACTAGAAGCACTGAGAGATGCGGCCCCCTCGCAGGGTCTGAATTTCCT
GCTGCTGTTCACAAAGATGCTTTTTATCTTTAACTTTTTGTTTTCCCCACTTCCGACCCCGGCGTTGATCTGCAT
CCTGACATTTGGAGCTGCCATCTTCTTGTGGCTGATCACCAGACCTCAACCCGTCTTACCTCTTCTTGACCTGAA
CAATCAGTCTGTGGGAATTGAGGGAGGAGCACGGAAGGGGGTTTCCCAGAAGAACAATGACCTAACAAGTTGCTG
CTTCTCAGATGCCAAGACTATGTATGAGGTTTTCCAAAGAGGACTCGCTGTGTCTGACAATGGGCCCTGCTTGGG
ATATAGAAAACCAAACCAGCCCTACAGATGGCTATCTTACAAACAGGTGTCTGATAGAGCAGAGTACCTGGGTTC
CTGTCTCTTGCATAAAGGTTATAAATCATCACCAGACCAGTTTGTCGGCATCTTTGCTCAGAATAGGCCAGAGTG
GATCATCTCCGAATTGGCTTGTTACACGTACTCTATGGTAGCTGTACCTCTGTATGACACCTTGGGACCAGAAGC
CATCGTACATATTGTCAACAAGGCTGATATCGCCATGGTGATCTGTGACACACCCCAAAAGGCATTGGTGCTGAT
AGGGAATGTAGAGAAAGGCTTCACCCCGAGCCTGAAGGTGATCATCCTTATGGACCCCTTTGATGATGACCTGAA
GCAAAGAGGGGAGAAGAGTGGAATTGAGATCTTATCCCTATATGATGCTGAGAACCTAGGCAAAGAGCACTTCAG
AAAACCTGTGCCTCCTAGCCCAGAAGACCTGAGCGTCATCTGCTTCACCAGTGGGACCACAGGTGACCCCAAAGG
AGCCATGATAACCCATCAAAATATTGTTTCAAATGCTGCTGCCTTTCTCAAATGTGTGGAGCATGCTTATGAGCC
CACTCCTGATGATGTGGCCATATCCTACCTCCCTCTGGCTCATATGTTTGAGAGGATTGTACAGGCTGTTGTGTA
CAGCTGTGGAGCCAGAGTTGGATTCTTCCAAGGGGATATTCGGTTGCTGGCTGACGACATGAAGACTTTGAAGCC
CACATTGTTTCCCGCGGTGCCTCGACTCCTTAACAGGATCTACGATAAGGTACAAAATGAGGCCAAGACACCCTT
GAAGAAGTTCTTGTTGAAGCTGGCTGTTTCCAGTAAATTCAAAGAGCTTCAAAAGGGTATCATCAGGCATGATAG
TTTCTGGGACAAGCTCATCTTTGCAAAGATCCAGGACAGCCTGGGCGGAAGGGTTCGTGTAATTGTCACTGGAGC
TGCCCCCATGTCCACTTCAGTCATGACATTCTTCCGGGCAGCAATGGGATGTCAGGTGTATGAAGCTTATGGTCA
AACAGAATGCACAGGTGGCTGTACATTTACATTACCTGGGGACTGGACATCAGGTCACGTTGGGGTGCCCCTGGC
TTGCAATTACGTGAAGCTGGAAGATGTGGCTGACATGAACTACTTTACAGTGAATAATGAAGGAGAGGTCTGCAT
CAAGGGTACAAACGTGTTCAAAGGATACCTGAAGGACCCTGAGAAGACACAGGAAGCCCTGGACAGTGATGGCTG
GCTTCACACAGGAGACATTGGTCGCTGGCTCCCGAATGGAACTCTGAAGATCATCGACCGTAAAAAGAACATTTT
CAAGCTGGCCCAAGGAGAATACATTGCACCAGAGAAGATAGAAAATATCTACAACAGGAGTCAACCAGTGTTACA
AATTTTTGTACACGGGGAGAGCTTACGGTCATCCTTAGTAGGAGTGGTGGTTCCTGACACAGATGTACTTCCCTC
ATTTGCAGCCAAGCTTGGGGTGAAGGGCTCCTTTGAGGAACTGTGCCAAAACCAAGTTGTAAGGGAAGCCATTTT
AGAAGACTTGCAGAAAATTGGGAAAGAAAGTGGCCTTAAAACTTTTGAACAGGTCAAAGCCATTTTTCTTCATCC
AGAGCCATTTTCCATTGAAAATGGGCTCTTGACACCAACATTGAAAGCAAAGCGAGGAGAGCTTTCCAAATACTT
TCGGACCCAAATTGACAGCCTGTATGAGCACATCCAGGATTAGGATAAGGTACTTAAGTACCTGCCGGCCCACTG
TGCACTGCTTGTGAGAAAATGGATTAAAAACTATTCTTACATTTGTTTTGCCTTTCCTCCTATTTTTTTTTAACC
TGTTAAACTCTAAAGCCATAGCTTTTGTTTTATATTGAGACATATAATGTGTAAACTTAGTTCCCAAATAAATCA
ATCCTGTCTTTCCCATCTTCGATGTTGCTAATATTAAGGCTTCAGGGCTACTTTTATCAACATGCCTGTCTTCAA
GATCCCAGTTTATGTTCTGTGTCCTTCCTCATGATTTCCAACCTTAATACTATTAGTAACCACAAGTTCAAGGGT
CAAAGGGACCCTCTGTGCCTTCTTCTTTGTTTTGTGATAAACATAACTTGCCAACAGTCTCTATGCTTATTTACA
TCTTCTACTGTTCAAACTAAGAGATTTTTAAATTCTGAAAAACTGCTTACAATTCATGTTTTCTAGCCACTCCAC
AAACCACTAAAATTTTAGTTTTAGCCTATCACTCATGTCAATCATATCTATGAGACAAATGTCTCCGATGCTCTT
CTGCGTAAATTAAATTGTGTACTGAAGGGAAAAGTTTGATCATACCAAACATTTCCTAAACTCTCTAGTTAGATA
TCTGACTTGGGAGTATTAAAAATTGGGTCTATGACATACTGTCCAAAAGGAATGCTGTTCTTAAAGCATTATTTA
CAGTAGGAACTGGGGAGTAAATCTGTTCCCTACAGTTTGCTGCTGAGCTGGAAGCTGTGGGGGAAGGAGTTGACA
GGTGGGCCCAGTGAACTTTTCCAGTAAATGAAGCAAGCACTGAATAAAAACCTCCTGAACTGGGAACAAAGATCT
ACAGGCAAGCAAGATGCCCACACAACAGGCTTATTTTCTGTGAAGGAACCAACTGATCTCCCCCACCCTTGGATT
AGAGTTCCTGCTCTACCTTACCCACAGATAACACATGTTGTTTCTACTTGTAAATGTAAAGTCTTTAAAATAAAC
TATTACAGATAAAAAA

FIGURE 52

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA60775

<subunit 1 of 1, 739 aa, 1 stop

<MW: 82263, pI: 7.55, NX(S/T): 3

MDALKPPCLWRNHERGKKDRDSCGRKNSEPGSPHSLEALRDAAPSQGLNFLLLFTKMLFIFN
FLFSPLPTPALICILTFGAAIFLWLITRPQPVLPLLDLNNQSVGIEGGARKGVSQKNNDLTS
CCFSDAKTMYEVFQRGLAVSDNGPCLGYRKPNQPYRWLSYKQVSDRAEYLGSCLLHKGYKSS
PDQFVGIFAQNRPEWIISELACYTYSMVAVPLYDTLGPEAIVHIVNKADIAMVICDTPQKAL
VLIGNVEKGFTPSLKVIILMDPFDDDLKQRGEKSGIEILSLYDAENLGKEHFRKPVPPSPED
LSVICFTSGTTGDPKGAMITHQNIVSNAAAFLKCVEHAYEPTPDDVAISYLPLAHMFERIVQ
AVVYSCGARVGFFQGDIRLLADDMKTLKPTLFPAVPRLLNRIYDKVQNEAKTPLKKFLLKLA
VSSKFKELQKGIIRHDSFWDKLIFAKIQDSLGGRVRVIVTGAAPMSTSVMTFFRAAMGCQVY
EAYGQTECTGGCTFTLPGDWTSGHVGVPLACNYVKLEDVADMNYFTVNNEGEVCIKGTNVFK
GYLKDPEKTQEALDSDGWLHTGDIGRWLPNGTLKIIDRKKNIFKLAQGEYIAPEKIENIYNR
SQPVLQIFVHGESLRSSLVGVVVPDTDVLPSFAAKLGVKGSFEELCQNQVVREAILEDLQKI
GKESGLKTFEQVKAIFLHPEPFSIENGLLTPTLKAKRGELSKYFRTQIDSLYEHIQD

Important features:

Type II transmembrane domain:

amino acids 61-80

Putative AMP-binding domain signature.

amino acids 314-325

N-glycosylation site.

amino acids 102-105, 588-591 and 619-622

FIGURE 53

GGAGGCGGAGGCCGCGGCGAGCCGGGCCGAGCAGTGAGGGCCCTAGCGGGGCCCGAGCGGGG
CCCGGGGCCCCTAAGCCATTCCTGAAGTCATGGGCTGGCCAGGACATTGGTGACCCGCCAAT
CCGGT**ATG**GACGACTGGAAGCCCAGCCCCCTCATCAAGCCCTTTGGGGCTCGGAAGAAGCGG
AGCTGGTACCTTACCTGGAAGTATAAACTGACAAACCAGCGGGCCCTGCGGAGATTCTGTCA
GACAGGGGCCGTGCTTTTCCTGCTGGTGACTGTCATTGTCAATATCAAGTTGATCCTGGACA
CTCGGCGAGCCATCAGTGAAGCCAATGAAGACCCAGAGCCAGAGCAAGACTATGATGAGGCC
CTAGGCCGCCTGGAGCCCCCACGGCGCAGAGGCAGTGGTCCCCGGCGGGTCCTGGACGTAGA
GGTGTATTCAAGTCGCAGCAAAGTATATGTGGCAGTGGATGGCACCACGGTGCTGGAGGATG
AGGCCCGGGAGCAGGGCCGGGGCATCCATGTCATTGTCCTCAACCAGGCCACGGGCCACGTG
ATGGCAAAACGTGTGTTTGACACGTACTCACCTCATGAGGATGAGGCCATGGTGCTATTCCT
CAACATGGTAGCGCCCGGCCGAGTGCTCATCTGCACTGTCAAGGATGAGGGCTCCTTCCACC
TCAAGGACACAGCCAAGGCTCTGCTGAGGAGCCTGGGCAGCCAGGCTGGCCCTGCCCTGGGC
TGGAGGGACACATGGGCCTTCGTGGGACGAAAAGGAGGTCCTGTCTTCGGGGAGAAACATTC
TAAGTCACCTGCCCTCTCTTCCTGGGGGGACCCAGTCCTGCTGAAGACAGATGTGCCATTGA
GCTCAGCAGAAGAGGCAGAGTGCCACTGGGCAGACACAGAGCTGAACCGTCGCCGCCGGCGC
TTCTGCAGCAAAGTTGAGGGCTATGGAAGTGTATGCAGCTGCAAGGACCCCACACCCATCGA
GTTCAGCCCTGACCCACTCCCAGACAACAAGGTCCTCAATGTGCCTGTGGCTGTCATTGCAG
GGAACCGACCCAATTACCTGTACAGGATGCTGCGCTCTCTGCTTTCAGCCCAGGGGGTGTCT
CCTCAGATGATAACAGTTTTCATTGACGGCTACTATGAGGAACCCATGGATGTGGTGGCACT
GTTTGGTCTGAGGGGCATCCAGCATACTCCCATCAGCATCAAGAATGCCCGCGTGTCTCAGC
ACTACAAGGCCAGCCTCACTGCCACTTTCAACCTGTTTCCGGAGGCCAAGTTTGCTGTGGTT
CTGGAAGAGGACCTGGACATTGCTGTGGATTTTTTCAGTTTCCTGAGCCAATCCATCCACCT
ACTGGAGGAGGATGACAGCCTGTACTGCATCTCTGCCTGGAATGACCAGGGGTATGAACACA
CGGCTGAGGACCCAGCACTACTGTACCGTGTGGAGACCATGCCTGGGCTGGGCTGGGTGCTC
AGGAGGTCCTTGTACAAGGAGGAGCTTGAGCCCAAGTGGCCTACACCGGAAAAGCTCTGGGA
TTGGGACATGTGGATGCGGATGCCTGAACAACGCCGGGGCCGAGAGTGCATCATCCCTGACG
TTTCCCGATCCTACCACTTTGGCATCGTCGGCCTCAACATGAATGGCTACTTTCACGAGGCC
TACTTCAAGAAGCACAAGTTCAACACGGTTCCAGGTGTCCAGCTCAGGAATGTGGACAGTCT
GAAGAAAGAAGCTTATGAAGTGGAAGTTCACAGGCTGCTCAGTGAGGCTGAGGTTCTGGACC
ACAGCAAGAACCCTTGTGAAGACTCTTTCCTGCCAGACACAGAGGGCCACACCTACGTGGCC
TTTATTCGAATGGAGAAAGATGATGACTTCACCACCTGGACCCAGCTTGCCAAGTGCCTCCA
TATCTGGGACCTGGATGTGCGTGGCAACCATCGGGGCCTGTGGAGATTGTTTCGGAAGAAGA
ACCACTTCCTGGTGGTGGGGGTCCCGGCTTCCCCCTACTCAGTGAAGAAGCCACCCTCAGTC
ACCCCAATTTTCCTGGAGCCACCCCCAAAGGAGGAGGGAGCCCCAGGAGCCCCAGAACAGAC
A**TGA**GACCTCCTCCAGGACCCTGCGGGGCTGGGTACTGTGTACCCCCAGGCTGGCTAGCCCT
TCCCTCCATCCTGTAGGATTTTGTAGATGCTGGTAGGGGCTGGGGCTACCTTGTTTTTAACA
TGAGACTTAATTACTAACTCCAAGGGGAGGGTTCCCCTGCTCCAACACCCCGTTCCTGAGTT
AAAAGTCTATTTATTTACTTCCTTGTTGGAGAAGGGCAGGAGAGTACCTGGGAATCATTACG
ATCCCTAGCAGCTCATCCTGCCCTTTGAATACCCTCACTTTCCAGGCCTGGCTCAGAATCTA
ACCTATTTATTGACTGTCCTGAGGGCCTTGAAAACAGGCCGAACCTGGAGGGCCTGGATTTC
TTTTTGGGCTGGAATGCTGCCCTGAGGGTGGGGCTGGCTCTTACTCAGGAAACTGCTGTGCC
CAACCCATGGACAGGCCCAGCTGGGGCCCACATGCTGACACAGACTCACTCAGAGACCCTTA
GACACTGGACCAGGCCTCCTCTCAGCCTTCTCTTTGTCCAGATTTCCAAAGCTGGATAAGTT
GGTCATTGATTAAAAAAGGAGAAGCCCTCTGGGAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 54

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA61185

><subunit 1 of 1, 660 aa, 1 stop

><MW: 75220, pI: 6.76, NX(S/T): 0

MDDWKPSPLIKPFGARKKRSWYLTWKYKLTNQRALRRFCQTGAVLFLLVTVIVNIKLILDTR
RAISEANEDPEPEQDYDEALGRLEPPRRRGSGPRRVLDVEVYSSRSKVYVAVDGTTVLEDEA
REQGRGIHVIVLNQATGHVMAKRVFDTYSPHEDEAMVLFLNMVAPGRVLICTVKDEGSFHLK
DTAKALLRSLGSQAGPALGWRDTWAFVGRKGGPVFGEKHSKSPALSSWGDPVLLKTDVPLSS
AEEAECHWADTELNRRRRRFCSKVEGYGSVCSCKDPTPIEFSPDPLPDNKVLNVPVAVIAGN
RPNYLYRMLRSLLSAQGVSPQMITVFIDGYYEEPMDVVALFGLRGIQHTPISIKNARVSQHY
KASLTATFNLFPEAKFAVVLEEDLDIAVDFFSFLSQSIHLLEEDDSLYCISAWNDQGYEHTA
EDPALLYRVETMPGLGWVLRRSLYKEELEPKWPTPEKLWDWDMWMRMPEQRRGRECIIPDVS
RSYHFGIVGLNMNGYFHEAYFKKHKFNTVPGVQLRNVDSLKKEAYEVEVHRLLSEAEVLDHS
KNPCEDSFLPDTEGHTYVAFIRMEKDDDFTTWTQLAKCLHIWDLDVRGNHRGLWRLFRKKNH
FLVVGVPASPYSVKKPPSVTPIFLEPPPKEEGAPGAPEQT

Important features of the protein:

Transmembrane domain:

amino acids 38-55

Homologous region to Mouse GNT1

amino acids 229-660

FIGURE 55

CGGACGCGTGGGCTGCTGGTGGGAAGGCCTAAAGAACTGGAAAGCCCACTCTCTTGGAACCACCACAC
CTGTTTAAAGAACCTAAGCACCATTTAAAGCCACTGGAAATTTGTTGTCTAGTGGTTGTGGGTGAATA
AAGGAGGGCAGA**ATG**GATGATTTCATCTCCATTAGCCTGCTGTCTCTGGCTATGTTGGTGGGATGTTA
CGTGGCCGGAATCATTCCCTTGGCTGTTAATTTCTCAGAGGAACGACTGAAGCTGGTGACTGTTTTGG
GTGCTGGCCTTCTCTGTGGAACTGCTCTGGCAGTCATCGTGCCTGAAGGAGTACATGCCCTTTATGAA
GATATTCTTGAGGGAAAACACCACCAAGCAAGTGAAACACATAATGTGATTGCATCAGACAAAGCAGC
AGAAAAATCAGTTGTCCATGAACATGAGCACAGCCACGACCACACACAGCTGCATGCCTATATTGGTG
TTTCCCTCGTTCTGGGCTTCGTTTTCATGTTGCTGGTGGACCAGATTGGTAACTCCCATGTGCATTCT
ACTGACGATCCAGAAGCAGCAAGGTCTAGCAATTCCAAAATCACCACCACGCTGGGTCTGGTTGTCCA
TGCTGCAGCTGATGGTGTTGCTTTGGGAGCAGCAGCATCTACTTCACAGACCAGTGTCCAGTTAATTG
TGTTTGTGGCAATCATGCTACATAAGGCACCAGCTGCTTTTGGACTGGTTTCCTTCTTGATGCATGCT
GGCTTAGAGCGGAATCGAATCAGAAAGCACTTGCTGGTCTTTGCATTGGCAGCACCAGTTATGTCCAT
GGTGACATACTTAGGACTGAGTAAGAGCAGTAAAGAAGCCCTTTCAGAGGTGAACGCCACGGGAGTGG
CCATGCTTTTCTCTGCCGGGACATTTCTTTATGTTGCCACAGTACATGTCCTCCCTGAGGTGGGCGGA
ATAGGGCACAGCCACAAGCCCGATGCCACGGGAGGGAGAGGCCTCAGCCGCCTGGAAGTGGCAGCCCT
GGTTCTGGGTTGCCTCATCCCTCTCATCCTGTCAGTAGGACACCAGCAT**TAA**ATGTTCAAGGTCCAGC
CTTGGTCCAGGGCCGTTTGCCATCCAGTGAGAACAGCCGGCACGTGACAGCTACTCACTTCCTCAGTC
TCTTGTCTCACCTTGCGCATCTCTACATGTATTCCTAGAGTCCAGAGGGGAGGTGAGGTTAAAACCTG
AGTAATGGAAAAGCTTTTAGAGTAGAAACACATTTACGTTGCAGTTAGCTATAGACATCCCATTGTGT
TATCTTTTAAAAGGCCCTTGACATTTTGCGTTTTAATATTTCTCTTAACCCTATTCTCAGGGAAGATG
GAATTTAGTTTTAAGGAAAAGAGGAGAACTTCATACTCACAATGAAATAGTGATTATGAAAATACAGT
GTTCTGTAATTAAGCTATGTCTCTTTCTTCTTAGTTTAGAGGCTCTGCTACTTTATCCATTGATTTTT
AACATGGTTCCCACCATGTAAGACTGGTGCTTTAGCATCTATGCCACATGCGTTGATGGAAGGTCATA
GCACCCACTCACTTAGATGCTAAAGGTGATTCTAGTTAATCTGGGATTAGGGTCAGGAAAATGATAGC
AAGACACATTGAAAGCTCTCTTTATACTCAAAAGAGATATCCATTGAAAAGGGATGTCTAGAGGGATT
TAAACAGCTCCTTTGGCACGTGCCTCTCTGAATCCAGCCTGCCATTCCATCAAATGGAGCAGGAGAGG
TGGGAGGAGCTTCTAAAGAGGTGACTGGTATTTTGTAGCATTCCTTGTCAAGTTCTCCTTTGCAGAAT
ACCTGTCTCCACATTCCTAGAGAGGAGCCAAGTTCTAGTAGTTTCAGTTCTAGGCTTTCCTTCAAGAA
CAGTCAGATCACAAAGTGTCTTTGGAAATTAAGGGATATTAAATTTTAAGTGATTTTTGGATGGTTAT
TGATATCTTTGTAGTAGCTTTTTTTAAAAGACTACCAAAATGTATGGTTGTCCTTTTTTTTTGTTTTT
TTTTTTTTTAATTATTTCTCTTAGCAGATCAGCAATCCCTCTAGGGACCTAAATACTAGGTCAGCTTT
GGCGACACTGTGTCTTCTCACATAACCACCTGTAGCAAGATGGATCATAAATGAGAAGTGTTTGCCTA
TTGATTTAAAGCTTATTGGAATCATGTCTCTTGTCTCTTCGTCTTTTCTTTGCTTTTCTTCTAACTTT
TCCCTCTAGCCTCTCCTCGCCACAATTTGCTGCTTACTGCTGGTGTTAATATTTGTGTGGGATGAATT
CTTATCAGGACAACCACTTCTCGAACTGTAATAATGAAGATAATAATATCTTTATTCTTTATCCCCTT
CAAAGAAATTACCTTTGTGTCAAATGCCGCTTTGTTGAGCCCTTAAAATACCACCTCCTCATGTGTAA
ATTGACACAATCACTAATCTGGTAATTTAAACAATTGAGATAGCAAAAGTGTTTAACAGACTAGGATA
ATTTTTTTTTCATATTTGCCAAAATTTTTGTAAACCCTGTCTTGTCAAATAAGTGTATAATATTGTAT
TATTAATTTATTTTTACTTTCTATACCATTTCAAAACACATTACACTAAGGGGGAACCAAGACTAGTT
TCTTCAGGGCAGTGGACGTAGTAGTTTGTAAAAACGTTTTCTATGACGCATAAGCTAGCATGCCTATG
ATTTATTTCCTTCATGAATTTGTCACTGGATCAGCAGCTGTGGAAATAAAGCTTGTGAGCCCTCTGCT
GGCCACAGTGAGGAAAGTAGCACAAATAGGATACAGTTGTATGTAGTCATTGGCAACAATTGCATACA
ATTTTACTACCAAGAGAAGGTATAGTATGGAAAGTCCAAATGACTTCCTTGATTGGATGTTAACAGCT
GACTGGTGTGAGACTTGAGGTTTCATCTAGTCCTTCAAAACTATATGGTTGCCTAGATTCTCTCTGGA
AACTGACTTTGTCAAATAAATAGCAGATTGTAGTGTCAAAAAAAA

FIGURE 56

MDDFISISLLSLAMLVGCYVAGIIPLAVNFSEERLKLVTVLGAGLLCGTALAVIVPEGVHAL
YEDILEGKHHQASETHNVIASDKAAEKSVVHEHEHSHDHTQLHAYIGVSLVLGFVFMLLVDQ
IGNSHVHSTDDPEAARSSNSKITTTLGLVVHAAADGVALGAAASTSQTSVQLIVFVAIMLHK
APAAFGLVSFLMHAGLERNRIRKHLLVFALAAPVMSMVTYLGLSKSSKEALSEVNATGVAML
FSAGTFLYVATVHVLPEVGGIGHSHKPDATGGRGLSRLEVAALVLGCLIPLILSVGHQH

Signal peptide:

amino acids 1-18

Transmembrane domain:

amino acids 37-56, 106-122, 211-230, 240-260, 288-304

FIGURE 57

GCTCGAGGCCGGCGGCGGCGGGAGAGCGACCCGGGCGGCCTCGTAGCGGGGCCCCGGATCCC

CGAGTGGCGGCCGGAGCCTCGAAAAGAGATTCTCAGCGCTGATTTTGAG**ATG**ATGGGCTTGG

GAAACGGGCGTCGCAGCATGAAGTCGCCGCCCCTCGTGCTGGCCGCCCTGGTGGCCTGCATC

ATCGTCTTGGGCTTCAACTACTGGATTGCGAGCTCCCGGAGCGTGGACCTCCAGACACGGAT

CATGGAGCTGGAAGGCAGGGTCCGCAGGGCGGCTGCAGAGAGAGGCGCCGTGGAGCTGAAGA

AGAACGAGTTCCAGGGAGAGCTGGAGAAGCAGCGGGAGCAGCTTGACAAAATCCAGTCCAGC

CACAACTTCCAGCTGGAGAGCGTCAACAAGCTGTACCAGGACGAAAAGGCGGTTTTGGTGAA

TAACATCACCACAGGTGAGAGGCTCATCCGAGTGCTGCAAGACCAGTTAAAGACCCTGCAGA

GGAATTACGGCAGGCTGCAGCAGGATGTCCTCCAGTTTCAGAAGAACCAGACCAACCTGGAG

AGGAAGTTCTCCTACGACCTGAGCCAGTGCATCAATCAGATGAAGGAGGTGAAGGAACAGTG

TGAGGAGCGAATAGAAGAGGTCACCAAAAAGGGGAATGAAGCTGTAGCTTCCAGAGACCTGA

GTGAAAACAACGACCAGAGACAGCAGCTCCAAGCCCTCAGTGAGCCTCAGCCCAGGCTGCAG

GCAGCAGGCCTGCCACACACAGAGGTGCCACAAGGGAAGGGAAACGTGCTTGGTAACAGCAA

GTCCCAGACACCAGCCCCCAGTTCCGAAGTGGTTTTGGATTCAAAGAGACAAGTTGAGAAAG

AGGAAACCAATGAGATCCAGGTGGTGAATGAGGAGCCTCAGAGGGACAGGCTGCCGCAGGAG

CCAGGCCGGGAGCAGGTGGTGGAAGACAGACCTGTAGGTGGAAGAGGCTTCGGGGGAGCCGG

AGAACTGGGCCAGACCCCACAGGTGCAGGCTGCCCTGTCAGTGAGCCAGGAAAATCCAGAGA

TGGAGGGCCCTGAGCGAGACCAGCTTGTCATCCCCGACGGACAGGAGGAGGAGCAGGAAGCT

GCCGGGGAAGGGAGAAACCAGCAGAAACTGAGAGGAGAAGATGACTACAACATGGATGAAAA

TGAAGCAGAATCTGAGACAGACAAGCAAGCAGCCCTGGCAGGGAATGACAGAAACATAGATG

TTTTTAATGTTGAAGATCAGAAAAGAGACACCATAAATTTACTTGATCAGCGTGAAAAGCGG

AATCATACACTC**TGA**ATTGAACTGGAATCACATATTTCACAACAGGGCCGAAGAGATGACTA

TAAAATGTTCATGAGGGACTGAATACTGAAAACTGTGAAATGTACTAAATAAAATGTACATCTGA

FIGURE 58

MMGLGNGRRSMKSPPLVLAALVACIIVLGFNYWIASSRSVDLQTRIMELEGRVRRAAAERGA
VELKKNEFQGELEKQREQLDKIQSSHNFQLESVNKLYQDEKAVLVNNITTGERLIRVLQDQL
KTLQRNYGRLQQDVLQFQKNQTNLERKFSYDLSQCINQMKEVKEQCEERIEEVTKKGNEAVA
SRDLSENNDQRQQLQALSEPQPRLQAAGLPHTEVPQGKGNVLGNSKSQTPAPSSEVVLDSKR
QVEKEETNEIQVVNEEPQRDRLPQEPGREQVVEDRPVGGRGFGGAGELGQTPQVQAALSVSQ
ENPEMEGPERDQLVIPDGQEEEQEAAGEGRNQQKLRGEDDYNMDENEAESETDKQAALAGND
RNIDVFNVEDQKRDTINLLDQREKRNHTL

Signal peptide:

amino acids 1-29

FIGURE 59

GG**ATG**CAGAAAGCCTCAGTGTTGCTCTTCCTGGCCTGGGTCTGCTTCCTCTTCTACGCTGGCATTGCCCTCTTCA
CCAGTGGCTTCCTGCTCACCCGTTTGGAGCTCACCAACCATAGCAGCTGCCAAGAGCCCCCAGGCCCTGGGTCCC
TGCCATGGGGGAGCCAAGGGAAACCTGGGGCCTGCTGGATGGCTTCCCGATTTTCGCGGGTTGTGTTGGTGCTGA
TAGATGCTCTGCGATTTGACTTCGCCCAGCCCCAGCATTCACACGTGCCTAGAGAGCCTCCTGTCTCCCTACCCT
TCCTGGGCAAACTAAGCTCCTTGCAGAGGATCCTGGAGATTCAGCCCCACCATGCCCGGCTCTACCGATCTCAGG
TTGACCCTCCTACCACCACCATGCAGCGCCTCAAGGCCCTCACCACTGGCTCACTGCCTACCTTTATTGATGCTG
GTAGTAACTTCGCCAGCCACGCCATAGTGGAAGACAATCTCATTAAGCAGCTCACCAGTGCAGGAAGGCGTGTAG
TCTTCATGGGAGATGATACCTGGAAAGACCTTTTCCCTGGTGCTTTCTCCAAAGCTTTCTTCTTCCCATCCTTCA
ATGTCAGAGACCTAGACACAGTGGACAATGGCATCCTGGAACACCTCTACCCCACCATGGACAGTGGTGAATGGG
ACGTGCTGATTGCTCACTTCCTGGGTGTGGACCACTGTGGCCACAAGCATGGCCCTCACCACCCTGAAATGGCCA
AGAAACTTAGCCAGATGGACCAGGTGATCCAGGGACTTGTGGAGCGTCTGGAGAATGACACACTGCTGGTAGTGG
CTGGGGACCATGGGATGACCACAAATGGAGACCATGGAGGGGACAGTGAGCTGGAGGTCTCAGCTGCTCTCTTTC
TGTATAGCCCCACAGCAGTCTTCCCCAGCACCCCACCAGAGGAGCCAGAGGTGATTCCTCAAGTTAGCCTTGTGC
CCACGCTGGCCCTGCTGCTGGGCCTGCCCATCCCATTTGGGAATATCGGGGAAGTGATGGCTGAGCTATTCTCAG
GGGGTGAGGACTCCCAGCCCCACTCCTCTGCTTTAGCCCAAGCCTCAGCTCTCCATCTCAATGCTCAGCAGGTGT
CCCGATTTCTTCATACCTACTCAGCTGCTACTCAGGACCTTCAAGCTAAGGAGCTTCATCAGCTGCAGAACCTCT
TCTCCAAGGCCTCTGCTGACTACCAGTGGCTTCTCCAGAGCCCCAAGGGGGCTGAGGCGACACTGCCGACTGTGA
TTGCTGAGCTGCAGCAGTTCCTGCGGGGAGCTCGGGCCATGTGCATCGAGTCTTGGGCTCGTTTCTCTCTGGTCC
GCATGGCGGGGGGTACTGCTCTCTTGGCTGCTTCCTGCTTTATCTGCCTGCTGGCATCTCAGTGGGCAATATCCC
CAGGCTTTCCATTCTGCCCTCTACTCCTGACACCTGTGGCCTGGGGCCTGGTTGGGGCCATAGCGTATGCTGGAC
TCCTGGGAACTATTGAGCTGAAGCTAGATCTAGTGCTTCTAGGGGCTGTGGCTGCAGTGAGCTCATTCCTCCCTT
TTCTGTGGAAAGCCTGGGCTGGCTGGGGGTCCAAGAGGCCCCTGGCAACCCTGTTTCCCATCCCTGGGCCCGTCC
TGTTACTCCTGCTGTTTCGCTTGGCTGTGTTCTTCTCTGATAGTTTTGTTGTAGCTGAGGCCAGGGCCACCCCCT
TCCTTTTGGGCTCATTCATCCTGCTCCTGGTTGTCCAGCTTCACTGGGAGGGCCAGCTGCTTCCACCTAAGCTAC
TCACAATGCCCCGCCTTGGCACTTCAGCCACAACAAACCCCCCACGGCACAATGGTGCATATGCCCTGAGGCTTG
GAATTGGGTTGCTTTTATGTACAAGGCTAGCTGGGCTTTTTCATCGTTGCCCTGAAGAGACACCTGTTTGCCACT
CCTCTCCCTGGCTGAGTCCTCTGGCATCCATGGTGGGTGGTCGAGCCAAGAATTTATGGTATGGAGCTTGTGTGG
CGGCGCTGGTGGCCCTGTTAGCTGCCGTGCGCTTGTGGCTTCGCCGCTATGGTAATCTCAAGAGCCCCGAGCCAC
CCATGCTCTTTGTGCGCTGGGGACTGCCCCTAATGGCATTGGGTACTGCTGCCTACTGGGCATTGGCGTCGGGGG
CAGATGAGGCTCCCCCCCGTCTCCGGGTCCTGGTCTCTGGGGCATCCATGGTGCTGCCTCGGGCTGTAGCAGGGC
TGGCTGCTTCAGGGCTCGCGCTGCTGCTCTGGAAGCCTGTGACAGTGCTGGTGAAGGCTGGGGCAGGCGCTCCAA
GGACCAGGACTGTCCTCACTCCCTTCTCAGGCCCCCCCACTTCTCAAGCTGACTTGGATTATGTGGTCCCTCAAA
TCTACCGACACATGCAGGAGGAGTTCCGGGGCCGGTTAGAGAGGACCAAATCTCAGGGTCCCCTGACTGTGGCTG
CTTATCAGTTGGGGAGTGTCTACTCAGCTGCTATGGTCACAGCCCTCACCCTGTTGGCCTTCCCACTTCTGCTGT
TGCATGCGGAGCGCATCAGCCTTGTGTTCCTGCTTCTGTTTCTGCAGAGCTTCCTTCTCCTACATCTGCTTGCTG
CTGGGATACCCGTCACCACCCCTGGTCCTTTTACTGTGCCATGGCAGGCAGTCTCGGCTTGGGCCCTCATGGCCA
CACAGACCTTCTACTCCACAGGCCACCAGCCTGTCTTTCCAGCCATCCATTGGCATGCAGCCTTCGTGGGATTCC
CAGAGGGTCATGGCTCCTGTACTTGGCTGCCTGCTTTGCTAGTGGGAGCCAACACCTTTGCCTCCCACCTCCTCT
TTGCAGTAGGTTGCCCACTGCTCCTGCTCTGGCCTTTCCTGTGTGAGAGTCAAGGGCTGCGGAAGAGACAGCAGC
CCCCAGGGAATGAAGCTGATGCCAGAGTCAGACCCGAGGAGGAAGAGGAGCCACTGATGGAGATGCGGCTCCGGG
ATGCGCCTCAGCACTTCTATGCAGCACTGCTGCAGCTGGGCCTCAAGTACCTCTTTATCCTTGGTATTCAGATTC
TGGCCTGTGCCTTGGCAGCCTCCATCCTTCGCAGGCATCTCATGGTCTGGAAAGTGTTTGCCCCTAAGTTCATAT
TTGAGGCTGTGGGCTTCATTGTGAGCAGCGTGGGACTTCTCCTGGGCATAGCTTTGGTGATGAGAGTGGATGGTG
CTGTGAGCTCCTGGTTCAGGCAGCTATTTCTGGCCCAGCAGAGG**TAG**CCTAGTCTGTGATTACTGGCACTTGGCT
ACAGAGAGTGCTGGAGAACAGTGTAGCCTGGCCTGTACAGGTACTGGATGATCTGCAAGACAGGCTCAGCCATAC
TCTTACTATCATGCAGCCAGGGGCCGCTGACATCTAGGACTTCATTATTCTATAATTCAGGACCACAGTGGAGTA
TGATCCCTAACTCCTGATTTGGATGCATCTGAGGGACAAGGGGGGCGGTCTCCGAAGTGGAATAAAATAGGCCGG
GCGTGGTGACTTGCACCTATAATCCCAGCACTTTGGGAGGCAGAGGTGGGAGGATTGCTTGGTCCCAGGAGTTCA
AGACCAGCCTGTGGAACATAACAAGACCCCGTCTCTACTATTTAAAAAAAAGTGTAATAAAATGATAATAT

FIGURE 60

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62809

<subunit 1 of 1, 1089 aa, 1 stop

<MW: 118699, pI: 8.49, NX(S/T): 2

MQKASVLLFLAWVCFLFYAGIALFTSGFLLTRLELTNHSSCQEPPGPGSLPWGSQGKPGACW
MASRFSRVVLVLIDALRFDFAQPQHSHVPREPPVSLPFLGKLSSLQRILEIQPHHARLYRSQ
VDPPTTTMQRLKALTTGSLPTFIDAGSNFASHAIVEDNLIKQLTSAGRRVVFMGDDTWKDLF
PGAFSKAFFFPSFNVRDLDTVDNGILEHLYPTMDSGEWDVLIAHFLGVDHCGHKHGPHHPEM
AKKLSQMDQVIQGLVERLENDTLLVVAGDHGMTTNGDHGGDSELEVSAALFLYSPTAVFPST
PPEEPEVIPQVSLVPTLALLLGLPIPFGNIGEVMAELFSGGEDSQPHSSALAQASALHLNAQ
QVSRFLHTYSAATQDLQAKELHQLQNLFSKASADYQWLLQSPKGAEATLPTVIAELQQFLRG
ARAMCIESWARFSLVRMAGGTALLAASCFICLLASQWAISPGFPFCPLLLTPVAWGLVGAIA
YAGLLGTIELKLDLVLLGAVAAVSSFLPFLWKAWAGWGSKRPLATLFPIPGPVLLLLLFRLA
VFFSDSFVVAEARATPFLLGSFILLLVVQLHWEGQLLPPKLLTMPRLGTSATTNPPRHNGAY
ALRLGIGLLLCTRLAGLFHRCPEETPVCHSSPWLSPLASMVGGRAKNLWYGACVAALVALLA
AVRLWLRRYGNLKSPEPPMLFVRWGLPLMALGTAAYWALASGADEAPPRLRVLVSGASMVLP
RAVAGLAASGLALLLWKPVTVLVKAGAGAPRTRTVLTPFSGPPTSQADLDYVVPQIYRHMQE
EFRGRLERTKSQGPLTVAAYQLGSVYSAAMVTALTLLAFPLLLLHAERISLVFLLLFLQSFL
LLHLLAAGIPVTTPGPFTVPWQAVSAWALMATQTFYSTGHQPVFPAIHWHAAFVGFPEGHGS
CTWLPALLVGANTFASHLLFAVGCPLLLLWPFLCESQGLRKRQQPPGNEADARVRPEEEEEP
LMEMRLRDAPQHFYAALLQLGLKYLFILGIQILACALAASILRRHLMVWKVFAPKFIFEAVG
FIVSSVGLLLGIALVMRVDGAVSSWFRQLFLAQQR

Important features:

Signal peptide:

amino acids 1-16

Transmembrane domains:

amino acids 317-341, 451-470, 481-500, 510-527, 538-555, 831-850, 1016-1034, 1052-1070

Leucine zipper pattern.

amino acids 843-864

N-glycosylation sites.

amino acids 37-40, 268-271

FIGURE 61

TGCCGCTGCCGCCGCTGCTGCTGTTGCTCCTGGCGGCGCCTTGGGGACGGGCAGTTCCCTGT
GTCTCTGGTGGTTTGCCTAAACCTGCAAACATCACCTTCTTATCCATCAACATGAAGA**ATG**T
CCTACAATGGACTCCACCAGAGGGTCTTCAAGGAGTTAAAGTTACTTACACTGTGCAGTATT
TCATCACAAATTGGCCCACCAGAGGTGGCACTGACTACAGATGAGAAGTCCATTTCTGTTGT
CCTGACAGCTCCAGAGAAGTGGAAGAGAAATCCAGAAGACCTTCCTGTTTCCATGCAACAAA
TATACTCCAATCTGAAGTATAACGTGTCTGTGTTGAATACTAAATCAAACAGAACGTGGTCC
CAGTGTGTGACCAACCACACGCTGGTGCTCACCTGGCTGGAGCCGAACACTCTTTACTGCGT
ACACGTGGAGTCCTTCGTCCCAGGGCCCCCTCGCCGTGCTCAGCCTTCTGAGAAGCAGTGTG
CCAGGACTTTGAAAGATCAATCATCAGAGTTCAAGGCTAAAATCATCTTCTGGTATGTTTTG
CCCATATCTATTACCGTGTTTCTTTTTTCTGTGATGGGCTATTCCATCTACCGATATATCCA
CGTTGGCAAAGAGAAACACCCAGCAAATTTGATTTTGATTTATGGAAATGAATTTGACAAAA
GATTCTTTGTGCCTGCTGAAAAAATCGTGATTAACTTTATCACCCTCAATATCTCGGATGAT
TCTAAAATTTCTCATCAGGATATGAGTTTACTGGGAAAAAGCAGTGATGTATCCAGCCTTAA
TGATCCTCAGCCCAGCGGGAACCTGAGGCCCCCTCAGGAGGAAGAGGAGGTGAAACATTTAG
GGTATGCTTCGCATTTGATGGAAATTTTTTGTGACTCTGAAGAAAACACGGAAGGTACTTCT
CTCACCCAGCAAGAGTCCCTCAGCAGAACAATACCCCCGGATAAAACAGTCATTGAATATGA
ATATGATGTCAGAACCACTGACATTTGTGCGGGGCCTGAAGAGCAGGAGCTCAGTTTGCAGG
AGGAGGTGTCCACACAAGGAACATTATTGGAGTCGCAGGCAGCGTTGGCAGTCTTGGGCCCG
CAAACGTTACAGTACTCATACACCCCTCAGCTCCAAGACTTAGACCCCCTGGCGCAGGAGCA
CACAGACTCGGAGGAGGGGCCGGAGGAAGAGCCATCGACGACCCTGGTCGACTGGGATCCCC
AAACTGGCAGGCTGTGTATTCCTTCGCTGTCCAGCTTCGACCAGGATTCAGAGGGCTGCGAG
CCTTCTGAGGGGGATGGGCTCGGAGAGGAGGGTCTTCTATCTAGACTCTATGAGGAGCCGGC
TCCAGACAGGCCACCAGGAGAAAATGAAACCTATCTCATGCAATTCATGGAGGAATGGGGGT
TATATGTGCAGATGGAAAAC**TGA**TGCCAACACTTCCTTTTGCCTTTTGTTTCCTGTGCAAAC
AAGTGAGTCACCCCTTTGATCCCAGCCATAAAGTACCTGGGATGAAAGAAGTTTTTTCCAGT
TTGTCAGTGTCTGTGAGAATTACTTATTTCTTTTCTCTATTCTCATAGCACGTGTGTGATTG
GTTCATGCATGTAGGTCTCTTAACAATGATGGTGGGCCTCTGGAGTCCAGGGGCTGGCCGGT
TGTTCTATGCAGAGAAAGCAGTCAATAAATGTTTGCCAGACTGGGTGCAGAATTTATTCAGG
TGGGTGT

FIGURE 62

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62815

<subunit 1 of 1, 442 aa, 1 stop

<MW: 49932, pI: 4.55, NX(S/T): 5

MSYNGLHQRVFKELKLLTLCSISSQIGPPEVALTTDEKSISVVLTAPEKWKRNPEDLPVSMQ
QIYSNLKYNVSVLNTKSNRTWSQCVTNHTLVLTWLEPNTLYCVHVESFVPGPPRRAQPSEKQ
CARTLKDQSSEFKAKIIFWYVLPISITVFLFSVMGYSIYRYIHVGKEKHPANLILIYGNEFD
KRFFVPAEKIVINFITLNISDDSKISHQDMSLLGKSSDVSSLNDPQPSGNLRPPQEEEEVKH
LGYASHLMEIFCDSEENTEGTSLTQQESLSRTIPPDKTVIEYEYDVRTTDICAGPEEQELSL
QEEVSTQGTLLESQAALAVLGPQTLQYSYTPQLQDLDPLAQEHTDSEEGPEEEPSTTLVDWD
PQTGRLCIPSLSSFDQDSEGCEPSEGDGLGEEGLLSRLYEEPAPDRPPGENETYLMQFMEEW
GLYVQMEN

Important features:

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 140-163

N-glycosylation sites.

amino acids 71-74, 80-83, 89-92, 204-207, 423-426

FIGURE 63

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGTCTCTGCGGGGAGACGCCAGCCTGCG
TCTGCC**ATG**GGGCTCGGGTTGAGGGGCTGGGGACGTCCTCTGCTGACTGTGGCCACCGCCCT
GATGCTGCCCGTGAAGCCCCCCGCAGGCTCCTGGGGGGCCCAGATCATCGGGGGCCACGAGG
TGACCCCCCACTCCAGGCCCTACATGGCATCCGTGCGCTTCGGGGGCCAACATCACTGCGGA
GGCTTCCTGCTGCGAGCCCGCTGGGTGGTCTCGGCCGCCCACTGCTTCAGCCACAGAGACCT
CCGCACTGGCCTGGTGGTGCTGGGCGCCCACGTCCTGAGTACTGCGGAGCCCACCCAGCAGG
TGTTTGGCATCGATGCTCTCACCACGCACCCCGACTACCACCCCATGACCCACGCCAACGAC
ATCTGCCTGCTGCGGCTGAACGGCTCTGCTGTCCTGGGCCCTGCAGTGGGGCTGCTGAGGCT
GCCAGGGAGAAGGGCCAGGCCCCCCACAGCGGGGACACGGTGCCGGGTGGCTGGCTGGGGCT
TCGTGTCTGACTTTGAGGAGCTGCCGCCTGGACTGATGGAGGCCAAGGTCCGAGTGCTGGAC
CCGGACGTCTGCAACAGCTCCTGGAAGGGCCACCTGACACTTACCATGCTCTGCACCCGCAG
TGGGGACAGCCACAGACGGGGCTTCTGCTCGGCCGACTCCGGAGGGCCCCTGGTGTGCAGGA
ACCGGGCTCACGGCCTCGTTTCCTTCTCGGGCCTCTGGTGCGGCGACCCCAAGACCCCCGAC
GTGTACACGCAGGTGTCCGCCTTTGTGGCCTGGATCTGGGACGTGGTTCGGCGGAGCAGTCC
CCAGCCCGGCCCCCTGCCTGGGACCACCAGGCCCCCAGGAGAAGCCGCC**TGA**GCCACAACCT
TGCGGCATGCAAATGAGATGGCCGCTCCAGGCCTGGAATGTTCCGTGGCTGGGCCCCACGGG
AAGCCTGATGTTCAGGGTTGGGGTGGACGGGCAGCGGTGGGGCACACCCATTCCACATGCA
AAGGGCAGAAGCAAACCCAGTAAAATGTTAACTGACAAAAAAAAAAAAAAAAAGAAA

FIGURE 64

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62845

><subunit 1 of 1, 283 aa, 1 stop

><MW: 30350, pI: 9.66, NX(S/T): 2

MGLGLRGWGRPLLTVATALMLPVKPPAGSWGAQIIGGHEVTPHSRPYMASVRFGGQHHCGGF
LLRARWVVSAAHCFSHRDLRTGLVVLGAHVLSTAEPTQQVFGIDALTTHPDYHPMTHANDIC
LLRLNGSAVLGPAVGLLRLPGRRARPPTAGTRCRVAGWGFVSDFEELPPGLMEAKVRVLDPD
VCNSSWKGHLTLTMLCTRSGDSHRRGFCSADSGGPLVCRNRAHGLVSFSGLWCGDPKTPDVY
TQVSAFVAWIWDVVRRSSPQPGPLPGTTRPPGEAA

Signal peptide:

amino acids 1-30

FIGURE 65

GAGCTACCCAGGCGGCTGGTGTGCAGCAAGCTCCGCGCCGACTCCGGACGCCTGACGCCTGA
CGCCTGTCCCCGGCCCGGC**ATG**AGCCGCTACCTGCTGCCGCTGTCGGCGCTGGGCACGGTAG
CAGGCGCCGCCGTGCTGCTCAAGGACTATGTCACCGGTGGGGCTTGCCCCAGCAAGGCCACC
ATCCCTGGGAAGACGGTCATCGTGACGGGCGCCAACACAGGCATCGGGAAGCAGACCGCCTT
GGAACTGGCCAGGAGAGGAGGCAACATCATCCTGGCCTGCCGAGACATGGAGAAGTGTGAGG
CGGCAGCAAAGGACATCCGCGGGGAGACCCTCAATCACCATGTCAACGCCCGGCACCTGGAC
TTGGCTTCCCTCAAGTCTATCCGAGAGTTTGCAGCAAAGATCATTGAAGAGGAGGAGCGAGT
GGACATTCTAATCAACAACGCGGGTGTGATGCGGTGCCCCCACTGGACCACCGAGGACGGCT
TCGAGATGCAGTTTGGCGTTAACCACCTGGGTCACTTTCTCTTGACAAACTTGCTGCTGGAC
AAGCTGAAAGCCTCAGCCCCTTCGCGGATCATCAACCTCTCGTCCCTGGCCCATGTTGCTGG
GCACATAGACTTTGACGACTTGAACTGGCAGACGAGGAAGTATAACACCAAAGCCGCCTACT
GCCAGAGCAAGCTCGCCATCGTCCTCTTCACCAAGGAGCTGAGCCGGCGGCTGCAAGGCTCT
GGTGTGACTGTCAACGCCCTGCACCCCGGCGTGGCCAGGACAGAGCTGGGCAGACACACGGG
CATCCATGGCTCCACCTTCTCCAGCACCACACTCGGGCCCATCTTCTGGCTGCTGGTCAAGA
GCCCCGAGCTGGCCGCCCAGCCCAGCACATACCTGGCCGTGGCGGAGGAACTGGCGGATGTT
TCCGGAAAGTACTTCGATGGACTCAAACAGAAGGCCCCGGCCCCCGAGGCTGAGGATGAGGA
GGTGGCCCGGAGGCTTTGGGCTGAAAGTGCCCGCCTGGTGGGCTTAGAGGCTCCCTCTGTGA
GGGAGCAGCCCCTCCCCAGA**TAA**CCTCTGGAGCAGATTTGAAAGCCAGGATGGCGCCTCCAG
ACCGAGGACAGCTGTCCGCCATGCCCGCAGCTTCCTGGCACTACCTGAGCCGGGAGACCCAG
GACTGGCGGCCGCCATGCCCGCAGTAGGTTCTAGGGGGCGGTGCTGGCCGCAGTGGACTGGC
CTGCAGGTGAGCACTGCCCCGGGCTCTGGCTGGTTCCGTCTGCTCTGCTGCCAGCAGGGGAG
AGGGGCCATCTGATGCTTCCCCTGGGAATCTAAACTGGGAATGGCCGAGGAGGAAGGGGCTC
TGTGCACTTGCAGGCCACGTCAGGAGAGCCAGCGGTGCCTGTCGGGGAGGGTTCCAAGGTGC
TCCGTGAAGAGCATGGGCAAGTTGTCTGACACTTGGTGGATTCTTGGGTCCCTGTGGGACCT
TGTGCATGCATGGTCCTCTCTGAGCCTTGGTTTCTTCAGCAGTGAGATGCTCAGAATAACTG
CTGTCTCCCATGATGGTGTGGTACAGCGAGCTGTTGTCTGGCTATGGCATGGCTGTGCCGGG
GGTGTTTGCTGAGGGCTTCCTGTGCCAGAGCCCAGCCAGAGAGCAGGTGCAGGTGTCATCCC
GAGTTCAGGCTCTGCACGGCATGGAGTGGGAACCCCACCAGCTGCTGCTACAGGACCTGGGA
TTGCCTGGGACTCCCACCTTCCTATCAATTCTCATGGTAGTCCAAACTGCAGACTCTCAAAC
TTGCTCATTT

FIGURE 66

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64842

><subunit 1 of 1, 331 aa, 1 stop

><MW: 35932, pI: 8.45, NX(S/T): 1

MSRYLLPLSALGTVAGAAVLLKDYVTGGACPSKATIPGKTVIVTGANTGIGKQTALELARRG
GNIILACRDMEKCEAAAKDIRGETLNHHVNARHLDLASLKSIREFAAKIIEEEERVDILINN
AGVMRCPHWTTEDGFEMQFGVNHLGHFLLTNLLLDKLKASAPSRIINLSSLAHVAGHIDFDD
LNWQTRKYNTKAAYCQSKLAIVLFTKELSRRLQGSGVTVNALHPGVARTELGRHTGIHGSTF
SSTTLGPIFWLLVKSPELAAQPSTYLAVAEELADVSGKYFDGLKQKAPAPEAEDEEVARRLW
AESARLVGLEAPSVREQPLPR

Signal peptide:

amino acids 1-17

FIGURE 67

GAAGTTCGCGAGCGCTGGC**ATG**TGGTCCTGGGGCGCGGCTGGCGGCGCTGCTGGCGGTGCTG
GCGCTCGGGACAGGAGACCCAGAAAGGGCTGCGGCTCGGGGCGACACGTTCTCGGCGCTGAC
CAGCGTGGCGCGCGCCCTGGCGCCCGAGCGCCGGCTGCTGGGGCTGCTGAGGCGGTACCTGC
GCGGGGAGGAGGCGCGGCTGCGGGACCTGACTAGATTCTACGACAAGGTACTTTCTTTGCAT
GAGGATTCAACAACCCCTGTGGCTAACCCTCTGCTTGCATTTACTCTCATCAAACGCCTGCA
GTCTGACTGGAGGAATGTGGTACATAGTCTGGAGGCCAGTGAGAACATCCGAGCTCTGAAGG
ATGGCTATGAGAAGGTGGAGCAAGACCTTCCAGCCTTTGAGGACCTTGAGGGAGCAGCAAGG
GCCCTGATGCGGCTGCAGGACGTGTACATGCTCAATGTGAAAGGCCTGGCCCGAGGTGTCTT
TCAGAGAGTCACTGGCTCTGCCATCACTGACCTGTACAGCCCCAAACGGCTCTTTTCTCTCA
CAGGGGATGACTGCTTCCAAGTTGGCAAGGTGGCCTATGACATGGGGGATTATTACCATGCC
ATTCCATGGCTGGAGGAGGCTGTCAGTCTCTTCCGAGGATCTTACGGAGAGTGGAAGACAGA
GGATGAGGCAAGTCTAGAAGATGCCTTGGATCACTTGGCCTTTGCTTATTTCCGGGCAGGAA
ATGTTTCGTGTGCCCTCAGCCTCTCTCGGGAGTTTCTTCTCTACAGCCCAGATAATAAGAGG
ATGGCCAGGAATGTCTTGAAATATGAAAGGCTCTTGGCAGAGAGCCCCAACCACGTGGTAGC
TGAGGCTGTCATCCAGAGGCCCAATATACCCCACCTGCAGACCAGAGACACCTACGAGGGGC
TATGTCAGACCCTGGGTTCCCAGCCCACTCTCTACCAGATCCCTAGCCTCTACTGTTCCTAT
GAGACCAATTCCAACGCCTACCTGCTGCTCCAGCCCATCCGGAAGGAGGTCATCCACCTGGA
GCCCTACATTGCTCTCTACCATGACTTCGTCAGTGACTCAGAGGCTCAGAAAATTAGAGAAC
TTGCAGAACCATGGCTACAGAGGTCAGTGGTGGCATCAGGGGAGAAGCAGTTACAAGTGGAG
TACCGCATCAGCAAAAGTGCCTGGCTGAAGGACACTGTTGACCCAAAACTGGTGACCCTCAA
CCACCGCATTGCTGCCCTCACAGGCCTTGATGTCCGGCCTCCCTATGCAGAGTATCTGCAGG
TGGTGAACTATGGCATCGGAGGACACTATGAGCCTCACTTTGACCATGCTACGTCACCAAGC
AGCCCCCTCTACAGAATGAAGTCAGGAAACCGAGTTGCAACATTTATGATCTATCTGAGCTC
GGTGGAAGCTGGAGGAGCCACAGCCTTCATCTATGCCAACCTCAGCGTGCCTGTGGTTAGGA
ATGCAGCACTGTTTTGGTGGAACCTGCACAGGAGTGGTGAAGGGGACAGTGACACACTTCAT
GCTGGCTGTCCTGTCCTGGTGGGAGATAAGTGGGTGGCCAACAAGTGGATACATGAGTATGG
ACAGGAATTCCGCAGACCCTGCAGCTCCAGCCCTGAAGAC**TGA**ACTGTTGGCAGAGAGAAGC
TGGTGGAGTCCTGTGGCTTTCCAGAGAAGCCAGGAGCCAAAAGCTGGGGTAGGAGAGGAGAA
AGCAGAGCAGCCTCCTGGAAGAAGGCCTTGTCAGCTTTGTCTGTGCCTCGCAAATCAGAGGC
AAGGGAGAGGTTGTTACCAGGGGACACTGAGAATGTACATTTGATCTGCCCCAGCCACGGAA
GTCAGAGTAGGATGCACAGTACAAAGGAGGGGGGAGTGGAGGCCTGAGAGGGAAGTTTCTGG
AGTTCAGATACTCTCTGTTGGGAACAGGACATCTCAACAGTCTCAGGTTCGATCAGTGGGTC
TTTTGGCACTTTGAACCTTGACCACAGGGACCAAGAAGTGGCAATGAGGACACCTGCAGGAG
GGGCTAGCCTGACTCCCAGAACTTTAAGACTTTCTCCCCACTGCCTTCTGCTGCAGCCCAAG
CAGGGAGTGTCCCCCTCCCAGAAGCATATCCCAGATGAGTGGTACATTATATAAGGATTTTT
TTTAAGTTGAAAACAACTTTCTTTTCTTTTTGTATGATGGTTTTTTAACACAGTCATTAAAA
ATGTTTATAAATCAAAA

FIGURE 68

MGPGARLAALLAVLALGTGDPERAAARGDTFSALTSVARALAPERRLLGLLRRYLRGEEARL
RDLTRFYDKVLSLHEDSTTPVANPLLAFTLIKRLQSDWRNVVHSLEASENIRALKDGYEKVE
QDLPAFEDLEGAARALMRLQDVYMLNVKGLARGVFQRVTGSAITDLYSPKRLFSLTGDDCFQ
VGKVAYDMGDYYHAIPWLEEAVSLFRGSYGEWKTEDEASLEDALDHLAFAYFRAGNVSCALS
LSREFLLYSPDNKRMARNVLKYERLLAESPNHVVAEAVIQRPNIPHLQTRDTYEGLCQTLGS
QPTLYQIPSLYCSYETNSNAYLLLQPIRKEVIHLEPYIALYHDFVSDSEAQKIRELAEPWLQ
RSVVASGEKQLQVEYRISKSAWLKDTVDPKLVTLNHRIAALTGLDVRPPYAEYLQVVNYGIG
GHYEPHFDHATSPSSPLYRMKSGNRVATFMIYLSSVEAGGATAFIYANLSVPVVRNAALFWW
NLHRSGEGDSDTLHAGCPVLVGDKWVANKWIHEYGQEFRRPCSSSPED

Signal peptide:

amino acids 1-19

FIGURE 69

GAGATAGGGAGTCTGGGTTTAAGTTCCTGCTCCATCTCAGGAGCCCCTGCTCCCACCCCTAG
GAAGCCACCAGACTCCACGGTGTGGGGCCAATCAGGTGGAATCGGCCCTGGCAGGTGGGGCC
ACGAGCGCTGGCTGAGGGACCGAGCCGGAGAGCCCCGGAGCCCCCGTAACCCGCGCGGGGAG
CGCCCAGG**ATG**CCGCGCGGGGACTCGGAGCAGGTGCGCTACTGCGCGCGCTTCTCCTACCTC
TGGCTCAAGTTTTCACTTATCATCTATTCCACCGTGTTCTGGCTGATTGGGGCCCTGGTCCT
GTCTGTGGGCATCTATGCAGAGGTTGAGCGGCAGAAATATAAAACCCTTGAAAGTGCCTTCC
TGGCTCCAGCCATCATCCTCATCCTCCTGGGCGTCGTCATGTTCATGGTCTCCTTCATTGGT
GTGCTGGCGTCCCTCCGTGACAACCTGTACCTTCTCCAAGCATTCATGTACATCCTTGGGAT
CTGCCTCATCATGGAGCTCATTGGTGGCGTGGTGGCCTTGACCTTCCGGAACCAGACCATTG
ACTTCCTGAACGACAACATTCGAAGAGGAATTGAGAACTACTATGATGATCTGGACTTCAAA
AACATCATGGACTTTGTTCAGAAAAAGTTCAAGTGCTGTGGCGGGGAGGACTACCGAGATTG
GAGCAAGAATCAGTACCACGACTGCAGTGCCCCTGGACCCCTGGCCTGTGGGGTGCCCTACA
CCTGCTGCATCAGGAACACGACAGAAGTTGTCAACACCATGTGTGGCTACAAAACTATCGAC
AAGGAGCGTTTCAGTGTGCAGGATGTCATCTACGTGCGGGGCTGCACCAACGCCGTGATCAT
CTGGTTCATGGACAACTACACCATCATGGCGTGCATCCTCCTGGGCATCCTGCTTCCCCAGT
TCCTGGGGGTGCTGCTGACGCTGCTGTACATCACCCGGGTGGAGGACATCATCATGGAGCAC
TCTGTCACTGATGGGCTCCTGGGGCCCGGTGCCAAGCCCAGCGTGGAGGCGGCAGGCACGGG
ATGCTGCTTGTGCTACCCCAAT**TAG**GGCCCAGCCTGCCATGGCAGCTCCAACAAGGACCGTC
TGGGATAGCACCTCTCAGTCAACATCGTGGGGCTGGACAGGGCTGCGGCCCCTCTGCCCACA
CTCAGTACTGACCAAAGCCAGGGCTGTGTGTGCCTGTGTGTAGGTCCCACGGCCTCTGCCTC
CCCAGGGAGCAGAGCCTGGGCCTCCCCTAAGAGGCTTTCCCCGAGGCAGCTCTGGAATCTGT
GCCCACCTGGGGCCTGGGGAACAAGGCCCTCCTTTCTCCAGGCCTGGGCTACAGGGGAGGGA
GAGCCTGAGGCTCTGCTCAGGGCCCATTTCATCTCTGGCAGTGCCTTGGCGGTGGTATTCAA
GGCAGTTTTGTAGCACCTGTAATTGGGGAGAGGGAGTGTGCCCCTCGGGGCAGGAGGGAAGG
GCATCTGGGGAAGGGCAGGAGGGAAGAGCTGTCCATGCAGCCACGCCCATGGCCAGGTTGGC
CTCTTCTCAGCCTCCCAGGTGCCTTGAGCCCTCTTGCAAGGGCGGCTGCTTCCTTGAGCCTA
GTTTTTTTTTACGTGATTTTTGTAACATTCATTTTTTTGTACAGATAACAGGAGTTTCTGAC
TAATCAAAGCTGGTATTTCCCCGCATGTCTTATTCTTGCCCTTCCCCCAACCAGTTTGTTAA
TCAAACAATAAAAACATGTTTTGTTTTGTTTTTAAAAAAAAA

FIGURE 70

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64863
><subunit 1 of 1, 294 aa, 1 stop
><MW: 33211, pI: 5.35, NX(S/T): 3
MPRGDSEQVRYCARFSYLWLKFSLIIYSTVFWLIGALVLSVGIYAEVERQKYKTLESAFLAP
AIILILLGVVMFMVSFIGVLASLRDNLYLLQAFMYILGICLIMELIGGVVALTFRNQTIDFL
NDNIRRGIENYYDDLDFKNIMDFVQKKFKCCGGEDYRDWSKNQYHDCSAPGPLACGVPYTCC
IRNTTEVVNTMCGYKTIDKERFSVQDVIYVRGCTNAVIIWFMDNYTIMACILLGILLPQFLG
VLLTLLYITRVEDIIMEHSVTDGLLGPGAKPSVEAAGTGCCLCYPN

Signal peptide:
amino acids 1-44

Transmembrane domains:
amino acids 22-42, 57-85, 93-116, 230-257

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 198 (SEQ ID NO:338), revealed some homology between the PRO1555 amino acid sequence and the following Dayhoff sequences: YKA4_CAEEL, AB014541_1, HVSX99518_2, SSU63019_1, GEN14286, MMU68267_1, XP2_XENLA, ICP4_HSV11, P_W40200, and AE001360_1.

Clone DNA73744-1665 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203322.

EXAMPLE 103: Isolation of cDNA clones Encoding Human PRO1485

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA44791". Based on the DNA44791 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1485.

PCR primers (2 forward and 2 reverse) were synthesized:

forward PCR primer 1: 5'CCCTCCAAGGATGACAAAGGCGC 3' (SEQ ID NO:341);

forward PCR primer 2: 5'GGTCAGCAGCTTTCTTGCCCTAAATCAGG 3' (SEQ ID NO:342);

reverse PCR primer 1: 5'ATCTCAGGCGGCATCCTGTCAGCC 3' (SEQ ID NO:343); and

reverse PCR primer 2: 5'GTGGATGCCTGCAAGAAGGTTGGG 3' (SEQ ID NO:344).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA44791 sequence which had the following nucleotide sequence:

hybridization probe 5'AGCTTTCTTGCCCTAAATCAGGCCAGCCTCATCAGTCGCTGTGAC 3' (SEQ ID NO:345)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1485 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human testis.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1485 (designated herein as DNA73746-1654 [Figure 199, SEQ ID NO:339]; and the derived protein sequence for PRO1485.

The entire coding sequence of PRO1485 is shown in Figure 199 (SEQ ID NO:339). Clone DNA73746-1654 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 151-153 and an apparent stop codon at nucleotide positions 595-597 of SEQ ID NO:339. The predicted polypeptide precursor is 148 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:340. The lysozyme C signature, CAAX box, and an N-gycosylation site are shown in Figure 200. Clone DNA73746-1654 has been deposited with ATCC and is assigned ATCC deposit no. 203411. The full-length PRO1485 protein shown in Figure 200 has an estimated molecular weight of about 16,896 daltons and a pI of about 6.05.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 200 (SEQ ID NO:340), revealed sequence identity

between the PRO1485 amino acid sequence and the following Dayhoff sequences: LYC_PHACO, P_R76684, 2HFL_Y, JC2144, JC5544, JC5555, JC5369, LYC2_PIG, P_R12113, and JC5380.

EXAMPLE 104: Isolation of cDNA clones Encoding Human PRO1564

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA67213. Based on the DNA67213 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1564.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (67213.f1) 5'-GGAGAGGTGGTGGCCATGGACAG-3' (SEQ ID NO:348)

reverse PCR primer (67213.r1) 5'-CTGTCACTGCAAGGAGCCAACACC-3' (SEQ ID NO:349)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA67213 sequence which had the following nucleotide sequence

hybridization probe (67213.p1)

5'-TATGTCGCTGCGAGGTGGTGAAAACCTCGAACTGTCTTTCAAGGC-3' (SEQ ID NO:350)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1564 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast carcinoma tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1564 (designated herein as DNA73760-1672 [Figure 201, SEQ ID NO:346]; and the derived protein sequence for PRO1564.

The entire nucleotide sequence of DNA73760-1672 is shown in Figure 201 (SEQ ID NO:346). Clone DNA73760-1672 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 462-464 and ending at the stop codon at nucleotide positions 2379-2381 (Figure 201). The predicted polypeptide precursor is 639 amino acids long (Figure 202). The full-length PRO1564 protein shown in Figure 202 has an estimated molecular weight of about 73,063 daltons and a pI of about 6.84. Analysis of the full-length PRO1564 sequence shown in Figure 202 (SEQ ID NO:347) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, a trasnmembrane domain from about amino acid 11 to about amino acid 36, potential N-glycosylation sites from about amino acid 107 to about amino acid 110 and from about amino acid 574 to about amino acid 577, a tyrosine kinase phosphorylation site from about amino acid 50 to about amino acid 57, potential N-myristolation sites from about amino acid 158 to about amino acid 163, from about amino acid 236 to about amino acid 241, from about amino acid 262 to about amino acid 267, from about amino acid 270 to about amino acid 275, from about amino acid 380 to about amino acid 385 and from about amino acid 513 to about amino acid 518, an amidation site from about amino acid 110 to about amino acid 113 and a prokaryotic membrane lipoprotein lipid attachment site from about amino acid 15 to about amino acid 25. Clone DNA73760-1672 has been deposited with ATCC on October 6, 1998 and is assigned ATCC deposit no.203314.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

alignment analysis of the full-length sequence shown in Figure 202 (SEQ ID NO:347), evidenced significant homology between the PRO1564 amino acid sequence and the following Dayhoff sequences: MMU73819_1, HSY08564_1, P_W34470, P_R66402, PAGT_HUMAN, CEGLY5B_1, CEGLY6A_1, CEGLY6B_1, AP000006_308 and E69322.

EXAMPLE 105: Isolation of cDNA clones Encoding Human PRO1755

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST Cluster No. 141872. This EST cluster sequence was then compared to a variety of ESTs from the databases listed above to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA55731".

In light of the sequence homology between the DNA55731 sequence and a sequence contained within Incyte EST no. 257323, the EST clone was purchased and the cDNA insert was obtained and sequenced. Incyte clone 257323 was derived from a library constructed using RNA isolated from the hNT2 cell line (Stratagene library no. STR9372310), which was derived from a human teratocarcinoma that exhibited properties characteristic of a committed neuronal precursor at an early stage of development. The sequence of this cDNA insert is shown in Figure 203 and is herein designated "DNA76396-1698". Alternatively, the DNA76396-1698 sequence can be obtained by preparing oligonucleotide probes and primers and isolating the sequence from an appropriate library (e.g. STR9372310).

The full length clone shown in Figure 203 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 58 to 60 and ending at the stop codon found at nucleotide positions 886 to 888 (Figure 203; SEQ ID NO:351). The predicted polypeptide precursor (Figure 204, SEQ ID NO:352) is 276 amino acids long. PRO1755 has a calculated molecular weight of approximately 29,426 daltons and an estimated pI of approximately 9.40. Additional features include: a signal peptide sequence at about amino acids 1-31; a transmembrane domain at about amino acids 178-198; a cAMP and cGMP-dependent protein kinase phosphorylation site at about amino acids 210-213; potential N-myristoylation sites at about amino acids 117-122, 154-149, and 214-219; and a cell attachment sequence at about amino acids 149-151.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 204 (SEQ ID NO:352), revealed some homology between the PRO1755 amino acid sequence and the following Dayhoff sequences: APG-BRANA, P_R37743, NAU88587_1, YHL1_EBV, P_W31855, CET10B10_4, AF039404_1, PRP1_HUMAN, AF038575_1, and AF053091_1.

Clone DNA76396-1698 was deposited with the ATCC on November 17, 1998, and is assigned ATCC deposit no. 203471.

EXAMPLE 106: Isolation of cDNA clones Encoding Human PRO1757

Use of the signal sequence algorithm described in Example 3 above allowed identification of three EST sequences from the Incyte database, designated Incyte EST clones no. 2007947, 2014962 and 1912034. These EST sequences were then clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA56054.

In light of the sequence homology between the DNA56054 sequence and a sequence contained within the Incyte EST clone no. 2007947, the Incyte EST clone no. 2007947 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 205 and is herein designated as DNA76398-1699.

Clone DNA76398-1699 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 59-61 and ending at the stop codon at nucleotide positions 422-424 (Figure 205). The predicted polypeptide precursor is 121 amino acids long (Figure 206). The full-length PRO1757 protein shown in Figure 206 has an estimated molecular weight of about 12,073 daltons and a pI of about 4.11. Analysis of the full-length PRO1757 sequence shown in Figure 206 (SEQ ID NO:354) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 91 to about amino acid 110, a glycosaminoglycan attachment site from about amino acid 44 to about amino acid 47, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 116 to about amino acid 119 and a potential N-myristolation site from about amino acid 91 to about amino acid 96. Clone DNA76398-1699 has been deposited with ATCC on November 17, 1998 and is assigned ATCC deposit no. 203474.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 206 (SEQ ID NO:354), evidenced significant homology between the PRO1757 amino acid sequence and the following Dayhoff sequences: JQ0964, COLL_HSVS7, HSU70136_1, AF003473_1, D89728_1, MTF1_MOUSE, AF029777_1, HSU88153_1 and P_W05321.

EXAMPLE 107: Isolation of cDNA clones Encoding Human PRO1758

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST cluster No. 20926. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) from the databases mentioned above, to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56260.

In light of the sequence homology between the DNA56260 sequence and a sequence contained within EST no. 2936330 from the LIFESEQ® database, the EST clone, which originated from a library constructed from thymus tissue of a fetus that died from anencephalus, was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 207 and is herein designated as DNA76399-1700.

The full length clone shown in Figure 207 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 78 to 80 and ending at the stop codon found at nucleotide positions 549-551 (Figure 207; SEQ ID NO:355). The predicted polypeptide precursor (Figure 208, SEQ ID NO:356) is 157 amino acids long. PRO1758 has a calculated molecular weight of approximately 17,681 daltons and an estimated pI of approximately 7.65. Additional features include: a signal peptide from about amino acids 1-15; a potential N-glycosylation site at about amino acids 24-27; a cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 27-30; a casein kinase II phosphorylation site at about amino acids 60-63; potential N-myristoylation sites at about amino acids 17-22, 50-55, 129-134, and 133-138; a cell attachment sequence at about amino acids 153-155; and a cytochrome c family heme-binding site signature at about amino acids 18-23.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 208 (SEQ ID NO:356), revealed significant homology between the PRO1758 amino acid sequence and Dayhoff sequence no AC005328_2. Homology was also found between the PRO1758 amino acid sequence and Dayhoff sequence no. CELC46F2_1.

Clone DNA76399-1700 was deposited with the ATCC on November 17, 1998 and is assigned ATCC deposit no. 203472.

EXAMPLE 108: Isolation of cDNA clones Encoding Human PRO1575

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as "DNA35699". Based on the DNA35699 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1575.

PCR primers (forward and reverse) were synthesized:

forward PCR primers: CCAGCAGTGCCCATACTCCATAGC (35699.f1; SEQ ID NO:359); TGACGAGTGGGATACACTGC (35699.f2; SEQ ID NO:360)

reverse PCR primer: GCTCTACGGAAACTTCTGCTGTGG (35699.r1; SEQ ID NO:361)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35699 sequence which had the following nucleotide sequence:

hybridization probe: ATTCCCAGGCGTGTCATTTGGGATCAGCACTGATTCTGAGGTTCTGACAC (35699.p1; SEQ ID NO:362)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1575 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human pancreatic tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1575 (designated herein as DNA76401-1683 [Figure 209, SEQ ID NO:357]; and the derived protein sequence for PRO1575.

The entire coding sequence of PRO1575 is shown in Figure 209 (SEQ ID NO:357). Clone DNA76401-1683 contains a single open reading frame with an apparent translational initiation site at nucleotide positions

22-24 and an apparent stop codon at nucleotide positions 841-843. The predicted polypeptide precursor is 273 amino acids long. The full-length PRO1575 protein shown in Figure 210 has an estimated molecular weight of about 30,480 daltons and a pI of about 4.60. Additional features include: a signal peptide at about amino acids 1-20; a transmembrane domain at about amino acids 143-162; a potential N-glycosylation site at about amino acids 100-103; and potential N-myristoylation sites at about amino acids 84-89, 103-108, 154-159, and 201-206.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 210 (SEQ ID NO:358), revealed significant homology between the PRO1575 amino acid sequence and Dayhoff sequence A12005_1. Homology was also revealed between the PRO1575 amino acid sequence and the following additional Dayhoff sequences: P_P80615; P_R25297; P_R51696; A47300; PDI_DROME; P_R49829; P_R63807; DMALPADAP_1; and DRZNF6_1.

Clone DNA76401-1683 was deposited with the ATCC on October 20,1998, and is assigned ATCC deposit no. 203360.

EXAMPLE 109: Isolation of cDNA clones Encoding Human PRO1787

A consensus DNA sequence was assembled relative to other EST sequences using phrap to form an assembly as described in Example 1 above. This consensus sequence is designated herein "DNA45123 ". Based on homology of DNA45123 to Incyte EST 3618549 identified in the assembly, as well as other discoveries and information provided herein, the clone including this EST was purchased and sequenced. DNA sequencing of the clone gave the full-length DNA sequence for PRO1787 and the derived protein sequence for PRO1787.

The entire coding sequence of PRO1787 is included in Figure 211 (SEQ ID NO:363). Clone DNA76510-2504 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 163-165 and an apparent stop codon at nucleotide positions 970-972 of SEQ ID NO:363. The approximate locations of the signal peptide, transmembrane domain, N-glycosylation sites, N-myristoylation sites and a kinase phosphorylation site are indicated in Figure 212. The predicted polypeptide precursor is 269 amino acids long. Clone DNA76510-2504 has been deposited with the ATCC and is assigned ATCC deposit no. 203477. The full-length PRO1787 protein shown in Figure 212 has an estimated molecular weight of about 29,082 daltons and a pI of about 9.02.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 212 (SEQ ID NO:364), revealed sequence identity between the PRO1787 amino acid sequence and the following Dayhoff sequences: MYP0_RAT, MYP0_HUMAN, MYP0_BOVIN, GEN12838, HSSCN2B2_1, AF007783_1, HSU90716_1, P_W42015, XLU43330_1 and AF060231_1.

EXAMPLE 110: Isolation of cDNA clones Encoding Human PRO1781

Initial DNA sequences referred to herein as DNA58070 and DNA56340 were identified using a yeast screen, in a human SK-Lu-1 adenocarcinoma cell line cDNA library that preferentially represents the 5' ends of the primary cDNA clones. These sequences were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence is designated herein as "DNA59575".

Based on the DNA59575 consensus sequence, the following oligonucleotides, were synthesized for use

as probes to isolate a clone of the full-length coding sequence for PRO1781 from a human fetal lung cDNA library: TGGAAAAGAAGTCTGGTCAGAAGGTTTAGG (SEQ ID NO:367), CATTTGGCTTCATTCTCCTGCTCTG (SEQ ID NO:368), AAAACCTCAGAACAACTCATTTTGCACC (SEQ ID NO:369) and GTCTCACCATGGTTGCTCTTGCCAAATTGTGGGAAGCAGGG (SEQ ID NO:370).

The full length DNA76522-2500 clone shown in Figure 213 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 21 to 23 and ending at the stop codon found at nucleotide positions 1141-1143 (Figure 213; SEQ ID NO:365). The predicted polypeptide precursor (Figure 214, SEQ ID NO:366) is 373 amino acids long. PRO1781 has a calculated molecular weight of approximately 41,221 daltons and an estimated pI of approximately 8.54. Additional features include: a possible signal peptide at about amino acids 1-19; a transmembrane domain at about amino acids 39-60; a tyrosine phosphorylation site at about amino acids 228-236; potential N-myristoylation sites at about amino acids 16-21, 17-22, 43-48, 45-50, 47-52, 49-54, 53-58, 58-63, 59-64, 62-67, 126-131, and 142-147; amidation sites at about amino acids 22-25 and 280-283; and a prokaryotic membrane lipoprotein lipid attachment site at about amino acids 12-22.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 214 (SEQ ID NO:366), revealed some homology between the PRO1781 amino acid sequence and the following Dayhoff sequences: CEY4510D_5, AP000001_146, P_R10676, DAC_STRSQ, CEC40H5_5, P_R35204, KPU58495_1, KPN16781_1, AF010403_1, and AF056116_14.

Clone DNA76522-2500 was deposited with the ATCC on November 17, 1998, and is assigned ATCC deposit no. 203469.

EXAMPLE 111: Isolation of cDNA clones Encoding Human PRO1556

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST Cluster No. 103158, and also referred to herein as "DNA10398". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and the LIFESEQ® database, to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56417.

In light of the sequence homology between the DNA56417 sequence and a sequence contained within Incyte EST no. 959332, EST no. 959332 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 215 and is herein designated as DNA76529-1666.

The full length clone shown in Figure 215 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 85 to 87 and ending at the stop codon found at nucleotide positions 892 to 894 (Figure 215; SEQ ID NO:371). The predicted polypeptide precursor (Figure 216, SEQ ID NO:372) is 269 amino acids long. PRO1556 has a calculated molecular weight of approximately 28,004 daltons and an estimated pI of approximately 5.80. Additional features include: a signal peptide sequence at about amino acids 1-24; transmembrane domains at about amino acids 11-25 and 226-243; a potential N-

glycosylation site at about amino acids 182-185, potential cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 29-34, 35-39, 117-122, 121-126, 125-130, 154-159, 166-171, 241-246, 246-251, 247-252, 249-254, 250-255, 251-256, 252-257, 253-258, 254-259, 255-260, 256-261, 257-262, and 259-264.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 216 (SEQ ID NO:372), revealed some homology between the PRO1556 amino acid sequence and the following Dayhoff sequences: T8F5_4, R23B_MOUSE, CANS_HUMAN, P_W41640, DSU51091_1, TP2B_CHICK, DVU20660_1, S43296, P_R23962, and BRN1_HUMAN.

Clone DNA76529-1666 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203315.

EXAMPLE 112: Isolation of cDNA clones Encoding Human PRO1759

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated DNA10571. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from pooled eosinophils of allergic asthmatic patients. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57313.

In light of the sequence homology between the DNA57313 sequence and the Incyte EST 2434255, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 217 and is herein designated as DNA76531-1701.

The full length clone shown in Figure 217 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 125-127 and ending at the stop codon found at nucleotide positions 1475-1477 (Figure 217; SEQ ID NO:373). The approximate locations of the signal peptide and transmembrane domains are indicated in Figure 218, whereas the approximate locations for N-myristoylation sites, a lipid attachment site, an amidation site and a kinase phosphorylation site are indicated in Figure 218. The predicted polypeptide precursor (Figure 218, SEQ ID NO:374) is 450 amino acids long. PRO1759 has a calculated molecular weight of approximately 49,765 daltons and an estimated pI of approximately 8.14. Clone DNA76531-1701 was deposited with the ATCC on November 17, 1998 and is assigned ATCC deposit no. 203465.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 218 (SEQ ID NO:374), revealed sequence identity between the PRO1759 amino acid sequence and the following Dayhoff sequences: OPDE_PSEAE, TH11_TRYBB, S67684, RGT2_YEAST, S68362, ATSUGTRPR_1, P_W17836 (Patent application WO9715668-A2), F69587, A48076, and A45611.

EXAMPLE 113: Isolation of cDNA clones Encoding Human PRO1760

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a prostate tumor library. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA58798.

In light of the sequence homology between DNA58798 sequence and the Incyte EST 3358745, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 219 and is herein designated as DNA76532-1702.

The full length clone shown in Figure 219 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 60-62 and ending at the stop codon found at nucleotide positions 624-626 (Figure 219; SEQ ID NO:375). The predicted polypeptide precursor (Figure 220, SEQ ID NO:376) is 188 amino acids long. Motifs are further indicated in Figure 220. PRO1760 has a calculated molecular weight of approximately 21,042 daltons and an estimated pI of approximately 5.36. Clone DNA76532-1702 was deposited with the ATCC on November 17, 1998 and is assigned ATCC deposit no. 203473.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 220 (SEQ ID NO:376), revealed sequence identity between the PRO1760 amino acid sequence and the following Dayhoff sequences: CELT07F12_2, T22J18_16, ATF1C12_3, APE3_YEAST, P_W22471, SAU56908_1, SCPA_STRPY, ATAC00423817, SAPURCLUS_2 and AF041468_9.

EXAMPLE 114: Isolation of cDNA clones Encoding Human PRO1561

A consensus DNA sequence was assembled relative to other EST sequences using phrap and repeated cycles of BLAST and phrap to extend a sequence as far as possible using the EST sequences discussed above as described in Example 1 above. This consensus sequence is herein designated DNA40630. Based on the DNA40630 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1561.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (40630.f1) 5'-CTGCCTCCACTGCTCTGTGCTGGG-3' (SEQ ID NO:379)

reverse PCR primer (40630.r1) 5'-CAGAGCAGTGGATGTTCCCCTGGG-3' (SEQ ID NO:380)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40630 sequence which had the following nucleotide sequence

hybridization probe (40630.p1)

5'-CTGAACAAGATGGTCAAGCAAGTGACTGGGAAAATGCCCATCCTC-3' (SEQ ID NO:381)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1561 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tumor tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1561 (designated herein as DNA76538-1670 [Figure 221, SEQ ID NO:377]; and the derived protein sequence for PRO1561.

The entire nucleotide sequence of DNA76538-1670 is shown in Figure 221 (SEQ ID NO:377). Clone DNA76538-1670 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 29-31 and ending at the stop codon at nucleotide positions 377-379 (Figure 221). The predicted polypeptide precursor is 116 amino acids long (Figure 222). The full-length PRO1561 protein shown in Figure 222 has an estimated molecular weight of about 12,910 daltons and a pI of about 6.41. Analysis of the full-length PRO1561 sequence shown in Figure 222 (SEQ ID NO:378) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 17, a transmembrane domain from about amino acid 1 to about amino acid 24, a potential N-glycosylation site from about amino acid 86 to about amino acid 89, potential N-myristolation sites from about amino acid 20 to about amino acid 25 and from about amino acid 45 to about amino acid 50 and a phospholipase A2 histidine active site from about amino acid 63 to about amino acid 70. Clone DNA76538-1670 has been deposited with ATCC on October 6, 1998 and is assigned ATCC deposit no. 203313.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 222 (SEQ ID NO:378), evidenced significant homology between the PRO1561 amino acid sequence and the following Dayhoff sequences: P_R63053, P_R25416, P_R63055, P_P93363, P_R63046, PA2A_VIPAA, P_W58476, GEN13747, PA2X_HUMAN and PA2A_CRODU.

In addition to the above, a sequence homology search evidenced significant homology between the DNA40630 consensus sequence and Incyte EST clone no. 1921092. As such, Incyte EST clone no. 1921092 was purchased and the insert obtained and sequenced, thereby giving rise to the DNA76538-1670 sequence shown in Figure 221 (SEQ ID NO:377).

EXAMPLE 115: Isolation of cDNA clones Encoding Human PRO1567

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA47580. The DNA47580 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA57246".

In light of the sequence homology between the DNA57246 sequence and EST no. 1793996 from the

LIFESEQ™ database, the clone containing the EST no. 1793996, which originates from a library constructed from prostate tumor tissue, was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 223 (SEQ ID NO:382) and is herein designated as DNA76541-1675.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111, and a stop signal at nucleotide positions 643-645 (Fig. 223; SEQ ID NO:382). The predicted polypeptide precursor is 178 amino acids long has a calculated molecular weight of approximately 19,600 daltons and an estimated pI of approximately 5.89. Additional features include a signal peptide at about amino acids 1-22; a potential N-glycosylation site at about amino acids 167-170; a protein kinase C phosphorylation site at about amino acids 107-109; and potential N-myristoylation sites at about amino acids 46-51, 72-77, and 120-125.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 224 (SEQ ID NO:383), evidenced significant homology between the PRO1567 amino acid sequence and human colon specific gene CSG6 polypeptide designated Dayhoff sequence "P_W06549". Homology was also found between the PRO1567 amino acid sequence and the following additional Dayhoff sequences: HUAC002301_1, P_246880, A49685, SPBP_RAT, S42924, SPBP_MOUSE, I52115, MMU03711_1, and AF041468_31.

Clone DNA76541-1675 has been deposited with the ATCC on October 27, 1998, and is assigned ATCC deposit no. 203409.

EXAMPLE 116: Isolation of cDNA clones Encoding Human PRO1693

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA38251. Based on the DNA38251 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1693.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (38251.f1) 5'-CTGGGATCTGAACAGTTTCGGGGC-3' (SEQ ID NO:386)

reverse PCR primer (38251.r1) 5'-GGTCCCCAGGACATGGTCTGTCCC-3' (SEQ ID NO:387)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA38251 sequence which had the following nucleotide sequence

hybridization probe (38251.p1)

5'-GCTGAGTTTACATTTACGGTCTAACTCCCTGAGAACCATCCCTGTGCG-3' (SEQ ID NO:388)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1693 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1693 (designated herein as DNA77301-1708 [Figure 225, SEQ ID NO:384]; and the derived protein sequence for PRO1693.

The entire nucleotide sequence of DNA77301-1708 is shown in Figure 225 (SEQ ID NO:384). Clone

DNA77301-1708 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 508-510 and ending at the stop codon at nucleotide positions 2047-2049 (Figure 225). The predicted polypeptide precursor is 513 amino acids long (Figure 226). The full-length PRO1693 protein shown in Figure 226 has an estimated molecular weight of about 58,266 daltons and a pI of about 9.84. Analysis of the full-length PRO1693 sequence shown in Figure 226 (SEQ ID NO:385) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 33, a transmembrane domain from about amino acid 420 to about amino acid 442, potential N-glycosylation sites from about amino acid 126 to about amino acid 129, from about amino acid 357 to about amino acid 360, from about amino acid 496 to about amino acid 499 and from about amino acid 504 to about amino acid 507, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 465 to about amino acid 468, a tyrosine kinase phosphorylation site from about amino acid 136 to about amino acid 142 and potential N-myristolation sites from about amino acid 11 to about amino acid 16, from about amino acid 33 to about amino acid 38, from about amino acid 245 to about amino acid 250, from about amino acid 332 to about amino acid 337, from about amino acid 497 to about amino acid 502 and from about amino acid 507 to about amino acid 512. Clone DNA77301-1708 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no. 203407.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 226 (SEQ ID NO:385), evidenced significant homology between the PRO1693 amino acid sequence and the following Dayhoff sequences: AB007876_1, ALS_MOUSE, HSCHON03_1, P_R85889, AF062006_1, AB014462_1, A58532, MUSLRRPA_1, AB007865_1 and AF030435_1.

EXAMPLE 117: Isolation of cDNA clones Encoding Human PRO1784

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA43862. Based on the DNA43862 sequence, oligonucleotide probes were generated and used to screen a human fetal kidney library prepared as described in paragraph 1 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (f1) 5'-CTTTTCAGTGTCACCTCAGCGATCTC-3' (SEQ ID NO:391); and

reverse PCR primer (r1) 5'-CCAAAACATGGAGCAGGAACAGG-3' (SEQ ID NO:392).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA43862 sequence which had the following nucleotide sequence:

hybridization probe (p1)

5'-CCAGTTGGTGCTCTCGGACCTACCATGCGAAGAAGATGAAATGTGTG-3' (SEQ ID NO:393).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1784 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 68-70, and a stop signal at nucleotide positions 506-508 (Fig. 227; SEQ ID NO:389). The predicted polypeptide precursor is 146 amino acids long has a calculated molecular

weight of approximately 16,116 daltons and an estimated pI of approximately 4.99. The approximate locations of the signal peptide, transmembrane domain and N-myristoylation site are indicated in Figure 228. Clone DNA77303-2502 has been deposited with the ATCC and is assigned ATCC deposit no. 203479.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 228 (SEQ ID NO:390), evidenced sequence identity between the PRO1784 amino acid sequence and the following Dayhoff sequences: RNU87224_1, RNAF000114_1, P_W31947, S18038, AE001300_8, AF039833_1, P_W39833_1, P_W39788, HSU87223_1, NTU06712_1, and P_W31946.

EXAMPLE 118: Isolation of cDNA clones Encoding Human PRO1605

A cDNA clone (DNA77648-1688) encoding a native human PRO1605 polypeptide was identified by a yeast screen, in a human fetal kidney cDNA library that preferentially represents the 5' ends of the primary cDNA clones.

The full-length DNA77648-1688 clone shown in Figure 229 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 425-427 and ending at the stop codon at nucleotide positions 845-847 (Figure 229). The predicted polypeptide precursor is 140 amino acids long (Figure 230). The full-length PRO1605 protein shown in Figure 230 has an estimated molecular weight of about 15,668 daltons and a pI of about 10.14. Analysis of the full-length PRO1605 sequence shown in Figure 230 (SEQ ID NO:395) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 26. Clone DNA77648-1688 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no. 203408.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 230 (SEQ ID NO:395), evidenced significant homology between the PRO1605 amino acid sequence and the following Dayhoff sequences: GNT5_HUMAN, P_R48975, P_W22519, MM26SPROT_1, HSU86782_1, CH60_LEPIN, HMCT_HELPY, F65126, HIU08875_1 and P_R41724.

EXAMPLE 119: Isolation of cDNA clones Encoding Human PRO1788

The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Incyte Clone No. 2968304 was identified as a sequence of interest having a BLAST score of 70 or greater that did not encode known proteins. The nucleotide sequence of Incyte Clone No. 2968304 is designated herein as "DNA6612".

In addition, the DNA6612 sequence was extended using repeated cycles of BLAST and phrap (Phil Green, University of Washington, Seattle, Washington) to extend the sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as "DNA49648". Based on the DNA49648 consensus sequence, oligonucleotides were synthesized: 1) to identify

by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1788.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: CCCTGCCAGCCGAGAGCTTCACC (49648.f1; SEQ ID NO:398)

reverse PCR primer: GGTTGGTGCCCGAAAGGTCCAGC (49648.r1; SEQ ID NO:399)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA49648 sequence which had the following nucleotide sequence:

hybridization probe: CAACCCCAAGCTTAACTGGGCAGGAGCTGAGGTGTTTTCAGGCC (49648.p1; SEQ ID NO:400)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1788 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1788 (designated herein as DNA77652-2505 [Figure 231, SEQ ID NO:396]; and the derived protein sequence for PRO1788.

The entire coding sequence of PRO1788 is shown in Figure 231 (SEQ ID NO:396). Clone DNA77652-2505 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 64-66 and an apparent stop codon at nucleotide positions 1123-1125. The predicted polypeptide precursor is 353 amino acids long. The full-length PRO1788 protein shown in Figure 232 has an estimated molecular weight of about 37,847 daltons and a pI of about 6.80. Additional features of PRO1788 include: a signal peptide at about amino acids 1-16; transmembrane domains at about amino acids 215-232 and 287-304; potential N-glycosylation sites at about amino acids 74-77 and 137-140; a glycosaminoglycan attachment site at about amino acids 45-48; a tyrosine kinase phosphorylation site at about amino acids 318-325; N-myristoylation sites at about amino acids 13-18, 32-37, 88-93, 214-219, and 223-228; and a leucine zipper pattern at about amino acids 284-305.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 232 (SEQ ID NO:397), revealed significant homology between the PRO1788 amino acid sequence and the following Dayhoff sequences: AF030435_1; AF062006_1; DMTARTAN_1; GARP_HUMAN; S42799; P_R71294; HSU88879_1; DROWHEELER_1; A58532; and AF068920_1.

Clone DNA77652-2505 was deposited with the ATCC on November 17, 1998, and is assigned ATCC deposit no. 203480.

EXAMPLE 120: Isolation of cDNA clones Encoding Human PRO1801

A proprietary expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to the IL-19 protein. This EST sequence is Incyte EST clone no. 819592 and is herein designated DNA79293. Based on the DNA79293 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1801.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCCTGTGGTCTCCAGATTTCAGGCCTA-3' (SEQ ID NO:403)

reverse PCR primer 5'-AGTCCTCCTTAAGATTCTGATGTCAA-3' (SEQ ID NO:404)

RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1801 (designated herein as DNA83500-2506 [Figure 233, SEQ ID NO:401]; and the derived protein sequence for PRO1801.

The entire nucleotide sequence of DNA83500-2506 is shown in Figure 233 (SEQ ID NO:401). Clone DNA83500-2506 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111 and ending at the stop codon at nucleotide positions 892-894 (Figure 233). The predicted polypeptide precursor is 261 amino acids long (Figure 234). The full-length PRO1801 protein shown in Figure 234 has an estimated molecular weight of about 29,667 daltons and a pI of about 8.76. Analysis of the full-length PRO1801 sequence shown in Figure 234 (SEQ ID NO:402) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 42, cAMP- and cGMP-dependent protein kinase phosphorylation sites from about amino acid 192 to about amino acid 195 and from about amino acid 225 to about amino acid 228 and potential N-myristolation sites from about amino acid 42 to about amino acid 47, from about amino acid 46 to about amino acid 51 and from about amino acid 136 to about amino acid 141. Clone DNA83500-2506 has been deposited with ATCC on October 29, 1998 and is assigned ATCC deposit no. 203391.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 234 (SEQ ID NO:402), evidenced significant homology between the PRO1801 amino acid sequence and the following Dayhoff sequences: P_W37935, HGS_B477, P_R32277, IL10_MACFA, P_W46585, P_R39714, P_R71471, P_R10159, IL10_RAT and P_W57201.

EXAMPLE 121: Isolation of cDNA clones Encoding Human UCP4

EST databases, which included public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA), were searched for sequences having homologies to human UCP3. The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the UCP3 protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program AssemblLIGN and MacVector (Oxford Molecular Group, Inc.).

A DNA sequence ("fromDNA") was assembled relative to other EST sequences using AssemblLIGN software. In addition, the fromDNA sequence was extended using repeated cycles of BLAST and AssemblLIGN

to extend the sequence as far as possible using the sources of EST sequences discussed above. Based on this DNA sequence, oligonucleotides were synthesized to isolate a clone of the full-length coding sequences for UCP4 by PCR. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer CGCGGATCCCGTTATCGTCTTGCGCTACTGC (SEQ ID NO:407)

reverse PCR primer GCGGAATTCTTAAAATGGACTGACTCCACTCATC (SEQ ID NO:408)

RNA for construction of the cDNA libraries was isolated from brain tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clone isolated by PCR as described above gave the full-length DNA sequence for UCP4 (designated herein as DNA77568-1626 [Figure 235, SEQ ID NO:405] and the derived protein sequence for UCP4.

The entire coding sequence of UCP4 is shown in Figure 235 (SEQ ID NO:405). Clone DNA77568-1626 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 27-29, and an apparent stop codon at nucleotide positions 996-998. (See Figure 235; SEQ ID NO:405). The predicted polypeptide precursor is 323 amino acids long. It is presently believed that UCP4 is a membrane-bound protein and contains at least 6 transmembrane regions. These putative transmembrane regions in the UCP4 amino acid sequence are illustrated in Figure 236. Clone DNA77568-1626, contained in the pcDNA3 vector (Invitrogen) has been deposited with ATCC and is assigned ATCC deposit no. 203134. UCP4 polypeptide is obtained or obtainable by expressing the molecule encoded by the cDNA insert of the deposited ATCC 203134 vector. Digestion of the vector with BamHI and EcoRI restriction enzymes will yield an approximate 972 plus 34 bp insert. The full-length UCP4 protein shown in Figure 236 has an estimated molecular weight of about 36,061 daltons and a pI of about 9.28.

EXAMPLE 122: Isolation of cDNA clones Encoding Human PRO193

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. Based on this consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO193.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GTTTGAGGAAGCTGGGATAC-3' (SEQ ID NO:411); and

reverse PCR primer 5'-CCAAACTCGAGCACCTGTTC-3' (SEQ ID NO:412).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus sequence which

had the following nucleotide sequence:

hybridization probe

5'-ATGGCAGGCTTCCTAGATAATTTTCGTTGGCCAGAATGTG-3' (SEQ ID NO:413).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO193 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human retina tissue (LIB94).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO193 [herein designated as DNA23322-1393] (SEQ ID NO:409) and the derived protein sequence for PRO193.

The entire nucleotide sequence of DNA23322-1393 is shown in Figure 237 (SEQ ID NO:409). Clone DNA23322-1393 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 138-140 and ending at the stop codon at nucleotide positions 612-614 (Figure 237). The predicted polypeptide precursor is 158 amino acids long (Figure 238). The full-length PRO193 protein shown in Figure 238 has an estimated molecular weight of about 17,936 and a pI of about 5.32. Clone DNA23322-1393 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Still analyzing the amino acid sequence of SEQ ID NO:410, transmembrane domains are at about amino acids 23-42, 60-80, 97-117 and 128-148 of SEQ ID NO:410. A cell attachment sequence is at about amino acids 81-83 of SEQ ID NO:410. A peroxidase proximal heme-ligand domain is at about amino acids 81-83 of SEQ ID NO:410. The corresponding nucleotides can be routinely determined given the sequences provided herein.

EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1130

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA34360. Based on the DNA34360 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1130.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (34360.f1) 5'-GCCATAGTCACGACATGGATG-3' (SEQ ID NO:416)

forward PCR primer (34360.f2) 5'-GGATGGCCAGAGCTGCTG-3' (SEQ ID NO:417)

forward PCR primer (34360.f3) 5'-AAAGTACAAGTGTGGCCTCATCAAGC-3' (SEQ ID NO:418)

reverse PCR primer (34360.r1) 5'-TCTGACTCCTAAGTCAGGCAGGAG-3' (SEQ ID NO:419)

reverse PCR primer (34360.r2) 5'-ATTCTCTCCACAGACAGCTGGTTC'3' (SEQ ID NO:420)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA34360 sequence which had the following nucleotide sequence

hybridization probe (34360.p1)

5'-GTACAAGTGTGGCCTCATCAAGCCCTGCCCAGCCAACTACTTTGCG-3' (SEQ ID NO:421)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1130 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human aortic endothelial cell tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1130 (designated herein as DNA59814-1486 [Figure 239, SEQ ID NO:414]; and the derived protein sequence for PRO1130.

The entire nucleotide sequence of DNA59814-1486 is shown in Figure 239 (SEQ ID NO:414). Clone DNA59814-1486 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 312-314 and ending at the stop codon at nucleotide positions 984-986 (Figure 239). The predicted polypeptide precursor is 224 amino acids long (Figure 240). The full-length PRO1130 protein shown in Figure 240 has an estimated molecular weight of about 24,963 daltons and a pI of about 9.64. Analysis of the full-length PRO1130 sequence shown in Figure 240 (SEQ ID NO:415) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, an ATP/GTP-binding site motif A from about amino acid 184 to about amino acid 191 and a potential N-glycosylation site from about amino acid 107 to about amino acid 110. Clone DNA59814-1486 has been deposited with ATCC on October 20,1998 and is assigned ATCC deposit no. 203359.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 240 (SEQ ID NO:415), evidenced significant homology between the PRO1130 amino acid sequence and the following Dayhoff sequences: P_W06547, 216_HUMAN, D87120_1, MMU72677_1, LAU04889_1, and D69319.

EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1335

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA35727. Based on the DNA35727 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1335.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (35727.f1) 5'-GTAAAGTCGCTGGCCAGC-3' (SEQ ID NO:424)

forward PCR primer (35727.f2) 5'-CCCGATCTGCCTGCTGTA-3' (SEQ ID NO:425)

reverse PCR primer (35727.r1) 5'-CTGCACTGTATGGCCATTATTGTG-3' (SEQ ID NO:426)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35727 sequence which had the following nucleotide sequence

hybridization probe (35727.p1)

5'-CAGAAACCCATGATACCCTACTGAACACCGAATCCCCTGGAAGCC-3' (SEQ ID NO:427)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1335 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human retina tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1335 (designated herein as DNA62812-1594 [Figure 241, SEQ ID NO:422]; and the derived protein sequence for PRO1335.

The entire nucleotide sequence of DNA62812-1594 is shown in Figure 241 (SEQ ID NO:422). Clone DNA62812-1594 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 271-273 and ending at the stop codon at nucleotide positions 1282-1284 (Figure 241). The predicted polypeptide precursor is 337 amino acids long (Figure 242). The full-length PRO1335 protein shown in Figure 242 has an estimated molecular weight of about 37,668 daltons and a pI of about 6.27. Analysis of the full-length PRO1335 sequence shown in Figure 242 (SEQ ID NO:423) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, a transmembrane domain from about amino acid 291 to about amino acid 310, a potential N-glycosylation site from about amino acid 213 to about amino acid 216 and amino acid sequence blocks having homology to eukaryotic-type carbonic anhydrase proteins from about amino acid 197 to about amino acid 245, from about amino acid 104 to about amino acid 140 and from about amino acid 22 to about amino acid 69. Clone DNA62812-1594 has been deposited with ATCC on September 9, 1998 and is assigned ATCC deposit no. 203248.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 242 (SEQ ID NO:423), evidenced significant homology between the PRO1335 amino acid sequence and the following Dayhoff sequences: AF037335_1, I38013, PTPG_MOUSE, CAH2_HUMAN , 1CAC, CAH7_HUMAN, CAH3_HUMAN, CAH1_HUMAN, CAH5_HUMAN and P_R41746.

EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1329

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte Cluster No. 167544, also referred herein as "DNA10680". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was derived from a cDNA library constructed from RNA isolated from synovial membrane tissue removed from the elbow of a female with rheumatoid arthritis. The consensus sequence obtained therefrom is herein designated "DNA58836".

In light of the sequence homology between the DNA58836 sequence and a sequence contained within the Incyte EST clone no. 368774, EST clone 368774 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 243 and is herein designated as DNA66660-1585.

The full length clone shown in Figure 243 contained a single open reading frame with an apparent

translational initiation site at nucleotide positions 90 to 92 and ending at the stop codon found at nucleotide positions 717 to 719 (Figure 243; SEQ ID NO:428). The predicted polypeptide precursor (Figure 244, SEQ ID NO:429) is 209 amino acids long, with a signal sequence at about amino acids 1-16. PRO1329 has a calculated molecular weight of approximately 21,588 daltons and an estimated pI of approximately 5.50. Clone DNA66660-1585 was deposited with the ATCC on September 22, 1998 and is assigned ATCC deposit no. 203279.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 244 (SEQ ID NO:429), revealed some homology between the PRO1329 amino acid sequence and the following Dayhoff sequences: CELK06A9_3, PROA_XANCP, CXU21300_4, MTV037_17, SYN1_RAT, I56542, S60743, BNOLE3_1, AB001573_1, and P_P80671.

EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1550

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST sequence from the Merck database, designated CELT15B7_12, also referred herein as "DNA10022". This EST sequence was then compared to a variety of expressed sequence tag (EST) databases which included public and proprietary EST databases (e.g., GenBank and LIFESEQ®) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA55708".

In light of the sequence homology between the DNA55708 sequence and a sequence contained within Incyte EST no. 3411659, the EST clone 3411659 was purchased and the cDNA insert was obtained and sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 245 and is herein designated as "DNA76393-1664".

The full length clone shown in Figure 245 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 138 to 140 and ending at the stop codon found at nucleotide positions 867 to 869 (Figure 245; SEQ ID NO:430). The predicted polypeptide precursor (Figure 246, SEQ ID NO:431) is 243 amino acids long. Other features of the PRO1550 protein include: a signal sequence at about amino acids 1-30; a hydrophobic domain at about amino acids 195-217; and a potential N-glycosylation site at about amino acids 186-189. PRO1550 has a calculated molecular weight of approximately 26,266 daltons and an estimated pI of approximately 8.43. Clone DNA76393-1664 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203323.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 246 (SEQ ID NO:431), revealed some homology between the PRO1550 amino acid sequence and the following Dayhoff sequences: CELF59E12_11; CA24_ASCSU; AF018082_1; CA13_BOVIN; CA54_HUMAN; CA34_HUMAN; HUMCOL7A1X_1; P_W09643; AF053538_1; and HSEMCXIV2_1.

EXAMPLE 127: Use of PRO as a hybridization probe

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

EXAMPLE 128: Expression of PRO in *E. coli*

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., supra. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful

sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g $(NH_4)_2SO_4$, 0.71 g sodium citrate•2H2O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM $MgSO_4$) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

E. coli paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 129: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., supra. The resulting vector is called pRK5-PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 μg pRK5-PRO DNA is mixed with about 1 μg DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500 μl of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M $CaCl_2$. To this mixture is added, dropwise, 500 μl of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM $NaPO_4$, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 μCi/ml ^{35}S-cysteine and 200 μCi/ml ^{35}S-methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Somparyrac et al., Proc. Natl. Acad. Sci., 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 μg pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 μg/ml bovine insulin and 0.1 μg/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as $CaPO_4$ or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as ^{35}S-methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by Ni^{2+}-chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., Current Protocols of Molecular Biology, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., Nucl. Acids Res. 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect® (Quiagen), Dosper® or Fugene® (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3 x 10^{-7} cells are frozen in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 μm filtered PS20 with 5% 0.2 μm diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with 3 x 10^5 cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at 1.2 x 10^6 cells/mL. On day 0, the cell number pH ie determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 μm filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 μL of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 130: Expression of PRO in Yeast

The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 131: Expression of PRO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of

PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni^{2+}-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM $MgCl_2$; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni^{2+}-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A_{280} with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A_{280} baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni^{2+}-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His_{10}-tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 132: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, supra. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice

by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

EXAMPLE 133: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (*e.g.*, high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (*e.g.*, a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

EXAMPLE 134: Drug Screening

This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (I) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

EXAMPLE 135: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (*c.f.*, Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained

to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

EXAMPLE 136: Stimulation of Endothelial Cell Proliferation (Assay 8)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to stimulate adrenal cortical capillary endothelial cell (ACE) growth. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

Bovine adrenal cortical capillary endothelial (ACE) cells (from primary culture, maximum of 12-14 passages) were plated in 96-well plates at 500 cells/well per 100 microliter. Assay media included low glucose DMEM, 10% calf serum, 2 mM glutamine, and 1X penicillin/streptomycin/fungizone. Control wells included the following: (1) no ACE cells added; (2) ACE cells alone; (3) ACE cells plus VEGF (5 ng/ml); and (4) ACE cells plus FGF (5ng/ml). The control or test sample, (in 100 microliter volumes), was then added to the wells (at dilutions of 1%, 0.1% and 0.01%, respectively). The cell cultures were incubated for 6-7 days at 37°C/5% CO_2. After the incubation, the media in the wells was aspirated, and the cells were washed 1X with PBS. An acid phosphatase reaction mixture (100 microliter; 0.1M sodium acetate, pH 5.5, 0.1% Triton X-100, 10 mM p-nitrophenyl phosphate) was then added to each well. After a 2 hour incubation at 37°C, the reaction was stopped by addition of 10 microliters 1N NaOH. Optical density (OD) was measured on a microplate reader at 405 nm.

The activity of a PRO polypeptide was calculated as the fold increase in proliferation (as determined by the acid phosphatase activity, OD 405 nm) relative to (1) cell only background, and (2) relative to maximum stimulation by VEGF. VEGF (at 3-10 ng/ml) and FGF (at 1-5 ng/ml) were employed as an activity reference

for maximum stimulation. Results of the assay were considered "positive" if the observed stimulation was ≥ 50% increase over background. VEGF (5 ng/ml) control at 1% dilution gave 1.24 fold stimulation; FGF (5 ng/ml) control at 1% dilution gave 1.46 fold stimulation.

The following PRO polypeptides tested positive in this assay: PRO1244, PRO1286 and PRO1303.

EXAMPLE 137: Inhibitory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 67)

This example shows that one or more of the polypeptides of the invention are active as inhibitors of the proliferation of stimulated T-lymphocytes. Compounds which inhibit proliferation of lymphocytes are useful therapeutically where suppression of an immune response is beneficial.

The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Insitutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO_2) and then washed and resuspended to $3x10^6$ cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:l of test sample diluted to 1% or to 0.1%,

50 :l of irradiated stimulator cells, and

50 :l of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO_2 for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mC/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to $1x10^7$ cells/ml of assay media. The assay is then conducted as described above.

Any decreases below control is considered to be a positive result for an inhibitory compound, with decreases of less than or equal to 80% being preferred. However, any value less than control indicates an inhibitory effect for the test protein.

The following polypeptide tested positive in this assay: PRO1250, PRO1418 and PRO1410.

EXAMPLE 138: Stimulation of Heart Neonatal Hypertrophy (Assay 1)

This assay is designed to measure the ability of PRO polypeptides to stimulate hypertrophy of neonatal heart. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic

treatment of various cardiac insufficiency disorders.

Cardiac myocytes from 1-day old Harlan Sprague Dawley rats were obtained. Cells (180 μl at 7.5 x 10^4/ml, serum <0.1%, freshly isolated) are added on day 1 to 96-well plates previously coated with DMEM/F12 + 4% FCS. Test samples containing the test PRO polypeptide are added directly to wells on day 2 in 20 μL volumes. Cells are stained with crystal violet after an additional two days and scored visually by the next day. Incubator conditions require 5% CO_2.

Activity reference: phenylephrine at 1-100 μM, PGF-2 alpha at 0.1-1.0 μM, endothelin-1 at 1-10 nM, CT1 (LIF) at 1-10 nM. No PBS is included, since calcium concentration is critical for assay response. Assay media included: DMEM/F12 (with 2.44 gm bicarbonate), 10 μg/ml transferrin, 1 μg/ml insulin, 1 μg/ml aprotinin, 2 mmol/L glutamine, 100 U/ml penicillin G, 100 μg/ml streptomycin. Protein buffer containing mannitol (4%) gave a positive signal (score 3.5) at 1/10 (0.4%) and 1/100 (0.04%), but not at 1/1000 (0.004%). Therefore, the test sample buffer containing mannitol is not run. A secondary assay consists of measuring the ANP levels (ng/ml) by ELISA in conditioned media from the cells. An increase in the ANP message can be measured by PCR from cells after a few hours.

Results are assessed by visually observing cell size: a score = 3.5 or greater is considered positive for conditioned media; a score of 3.0 or greater is considered positive for purified protein.

The following purified PRO polypeptide was observed to stimulate neonatal heart hypertrophy in this assay: PRO1246.

EXAMPLE 139: Inhibition of Vascular Endothelial Growth Factor (VEGF) Stimulated Proliferation of Endothelial Cell Growth (Assay 9)

The ability of various PRO polypeptides to inhibit VEGF stimulated proliferation of endothelial cells was tested. Polypeptides testing positive in this assay are useful for inhibiting endothelial cell growth in mammals where such an effect would be beneficial, e.g., for inhibiting tumor growth.

Specifically, bovine adrenal cortical capillary endothelial cells (ACE) (from primary culture, maximum of 12-14 passages) were plated in 96-well plates at 500 cells/well per 100 microliter. Assay media included low glucose DMEM, 10% calf serum, 2 mM glutamine, and 1X penicillin/streptomycin/fungizone. Control wells included the following: (1) no ACE cells added; (2) ACE cells alone; (3) ACE cells plus 5 ng/ml FGF; (4) ACE cells plus 3 ng/ml VEGF; (5) ACE cells plus 3 ng/ml VEGF plus 1 ng/ml TGF-beta; and (6) ACE cells plus 3 ng/ml VEGF plus 5 ng/ml LIF. The test samples, poly-his tagged PRO polypeptides (in 100 microliter volumes), were then added to the wells (at dilutions of 1%, 0.1% and 0.01%, respectively). The cell cultures were incubated for 6-7 days at 37°C/5% CO_2. After the incubation, the media in the wells was aspirated, and the cells were washed 1X with PBS. An acid phosphatase reaction mixture (100 microliter; 0.1M sodium acetate, pH 5.5, 0.1% Triton X-100, 10 mM p-nitrophenyl phosphate) was then added to each well. After a 2 hour incubation at 37°C, the reaction was stopped by addition of 10 microliters 1N NaOH. Optical density (OD) was measured on a microplate reader at 405 nm.

The activity of PRO polypeptides was calculated as the percent inhibition of VEGF (3 ng/ml) stimulated proliferation (as determined by measuring acid phosphatase activity at OD 405 nm) relative to the cells without stimulation. TGF-beta was employed as an activity reference at 1 ng/ml, since TGF-beta blocks 70-90% of VEGF-stimulated ACE cell proliferation. The results are indicative of the utility of the PRO polypeptides in

cancer therapy and specifically in inhibiting tumor angiogenesis. Numerical values (relative inhibition) are determined by calculating the percent inhibition of VEGF stimulated proliferation by the PRO polypeptides relative to cells without stimulation and then dividing that percentage into the percent inhibition obtained by TGF-β at 1 ng/ml which is known to block 70-90% of VEGF stimulated cell proliferation. The results are considered positive if the PRO polypeptide exhibits 30% or greater inhibition of VEGF stimulation of endothelial cell growth (relative inhibition 30% or greater).

The following polypeptide tested positive in this assay: PRO1246.

EXAMPLE 140: Human Venous Endothelial Cell Calcium Flux Assay (Assay 68)

This assay is designed to determine whether PRO polypeptides show the ability to stimulate calcium flux in human umbilical vein endothelial cells (HUVEC, Cell Systems). Calcium influx is a well documented response upon binding of certain ligands to their receptors. A test compound that results in a positive response in the present calcium influx assay can be said to bind to a specific receptor and activate a biological signaling pathway in human endothelial cells. This will ultimately lead, for example, to cell division, inhibition of cell proliferation, endothelial tube formation, cell migration, apoptosis, etc.

Human venous umbilical vein endothelial cells (HUVEC, Cell Systems) in growth media (50:50 without glycine, 1% glutamine, 10mM Hepes, 10% FBS, 10 ng/ml bFGF), were plated on 96-well microtiter ViewPlates-96 (Packard Instrument Company Part #6005182) microtiter plates at a cell density of 2 x 10^4 cells/well. The day after plating, the cells were washed three times with buffer (HBSS plus 10 mM Hepes), leaving 100 μl/well. Then 100 μl/well of 8 μM Fluo-3 (2x) was added. The cells were incubated for 1.5 hours at 37°C/5% CO_2. After incubation, the cells were then washed 3x with buffer (described above) leaving 100 μl/well. Test samples of the PRO polypeptides were prepared on different 96-well plates at 5x concentration in buffer. The positive control corresponded to 50 μM ionomycin (5x); the negative control corresponded to Protein 32. Cell plate and sample plates were run on a FLIPR (Molecular Devices) machine. The FLIPR machine added 25 μl of test sample to the cells, and readings were taken every second for one minute, then every 3 seconds for the next three minutes.

The fluorescence change from baseline to the maximum rise of the curve (Δ change) was calculated, and replicates averaged. The rate of fluorescence increase was monitored, and only those samples which had a Δ change greater than 1000 and a rise within 60 seconds, were considered positive.

The following PRO polypeptides tested positive in this assay: PRO1246 and PRO1561.

EXAMPLE 141: Skin Vascular Permeability Assay (Assay 64)

This assay shows that certain polypeptides of the invention stimulate an immune response and induce inflammation by inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection of the animal. Compounds which stimulate an immune response are useful therapeutically where stimulation of an immune response is beneficial. This skin vascular permeability assay is conducted as follows. Hairless guinea pigs weighing 350 grams or more are anesthetized with ketamine (75-80 mg/Kg) and 5 mg/Kg xylazine intramuscularly (IM). A sample of purified polypeptide of the invention or a conditioned media test sample is injected intradermally onto the backs of the test animals with 100 μl per injection site. It is possible to have

about 10-30, preferably about 16-24, injection sites per animal. One μl of Evans blue dye (1% in physiologic buffered saline) is injected intracardially. Blemishes at the injection sites are then measured (mm diameter) at 1 hr and 6 hr post injection. Animals were sacrificed at 6 hrs after injection. Each skin injection site is biopsied and fixed in formalin. The skins are then prepared for histopathologic evaluation. Each site is evaluated for inflammatory cell infiltration into the skin. Sites with visible inflammatory cell inflammation are scored as positive. Inflammatory cells may be neutrophilic, eosinophilic, monocytic or lymphocytic. At least a minimal perivascular infiltrate at the injection site is scored as positve, no infiltrate at the site of injection is scored as negative.

The following polypeptide tested positive in this assay: PRO1283, PRO1325 and PRO1343.

EXAMPLE 142: Induction of c-fos in Endothelial Cells (Assay 34)

This assay is designed to determine whether PRO polypeptides show the ability to induce c-fos in endothelial cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

Human venous umbilical vein endothelial cells (HUVEC, Cell Systems) in growth media (50% Ham's F12 w/o GHT: low glucose, and 50% DMEM without glycine: with NaHCO3, 1% glutamine, 10 mM HEPES, 10% FBS, 10 ng/ml bFGF) were plated on 96-well microtiter plates at a cell density of $1x10^4$ cells/well. The day after plating, the cells were starved by removing the growth media and treating the cells with 100 μl/well test samples and controls (positive control = growth media; negative control = Protein 32 buffer = 10 mM HEPES, 140 mM NaCl, 4% (w/v) mannitol, pH 6.8). The cells were incubated for 30 minutes at 37°C, in 5% CO_2. The samples were removed, and the first part of the bDNA kit protocol (Chiron Diagnostics, cat. #6005-037) was followed, where each capitalized reagent/buffer listed below was available from the kit.

Briefly, the amounts of the TM Lysis Buffer and Probes needed for the tests were calculated based on information provided by the manufacturer. The appropriate amounts of thawed Probes were added to the TM Lysis Buffer. The Capture Hybridization Buffer was warmed to room temperature. The bDNA strips were set up in the metal strip holders, and 100 μl of Capture Hybridization Buffer was added to each b-DNA well needed, followed by incubation for at least 30 minutes. The test plates with the cells were removed from the incubator, and the media was gently removed using the vacuum manifold. 100 μl of Lysis Hybridization Buffer with Probes were quickly pipetted into each well of the microtiter plates. The plates were then incubated at 55°C for 15 minutes. Upon removal from the incubator, the plates were placed on the vortex mixer with the microtiter adapter head and vortexed on the #2 setting for one minute. 80 μl of the lysate was removed and added to the bDNA wells containing the Capture Hybridization Buffer, and pipetted up and down to mix. The plates were incubated at 53°C for at least 16 hours.

On the next day, the second part of the bDNA kit protocol was followed. Specifically, the plates were removed from the incubator and placed on the bench to cool for 10 minutes. The volumes of additions needed were calculated based upon information provided by the manufacturer. An Amplifier Working Solution was

prepared by making a 1:100 dilution of the Amplifier Concentrate (20 fm/μl) in AL Hybridization Buffer. The hybridization mixture was removed from the plates and washed twice with Wash A. 50 μl of Amplifier Working Solution was added to each well and the wells were incubated at 53°C for 30 minutes. The plates were then removed from the incubator and allowed to cool for 10 minutes. The Label Probe Working Solution was prepared by making a 1:100 dilution of Label Concentrate (40 pmoles/μl) in AL Hybridization Buffer. After the 10-minute cool-down period, the amplifier hybridization mixture was removed and the plates were washed twice with Wash A. 50 μl of Label Probe Working Solution was added to each well and the wells were incubated at 53°C for 15 minutes. After cooling for 10 minutes, the Substrate was warmed to room temperature. Upon addition of 3 μl of Substrate Enhancer to each ml of Substrate needed for the assay, the plates were allowed to cool for 10 minutes, the label hybridization mixture was removed, and the plates were washed twice with Wash A and three times with Wash D. 50 μl of the Substrate Solution with Enhancer was added to each well. The plates were incubated for 30 minutes at 37°C and RLU was read in an appropriate luminometer.

The replicates were averaged and the coefficient of variation was determined. The measure of activity of the fold increase over the negative control (Protein 32/HEPES buffer described above) value was indicated by chemiluminescence units (RLU). The results are considered positive if the PRO polypeptide exhibits at least a two-fold value over the negative buffer control. Negative control = 1.00 RLU at 1.00% dilution. Positive control = 8.39 RLU at 1.00% dilution.

The following PRO polypeptides tested positive in this assay: PRO1274, PRO1294, PRO1304 and PRO1130.

EXAMPLE 143: Gene Amplification

This example shows that the PRO1295-, PRO1293-, PRO1265-, PRO1303-, PRO1269-, PRO1410-, PRO1317-, PRO1780-, PRO1555-, PRO1755-, PRO1558-, PRO1759- and PRO1788-encoding genes are amplified in the genome of certain human lung, colon and/or breast cancers and/or cell lines. Amplification is associated with overexpression of the gene product, indicating that the polypeptides are useful targets for therapeutic intervention in certain cancers such as colon, lung, breast and other cancers. Therapeutic agents may take the form of antagonists of PRO1295, PRO1293, PRO1265, PRO1303, PRO1269, PRO1410, PRO1317, PRO1780, PRO1555, PRO1755, PRO1558, PRO1759 and PRO1788 polypeptides, for example, murine-human chimeric, humanized or human antibodies against a PRO1295, PRO1293, PRO1265, PRO1303, PRO1269, PRO1410, PRO1317, PRO1780, PRO1555, PRO1755, PRO1558, PRO1759 or PRO1788 polypeptide.

The starting material for the screen was genomic DNA isolated from a variety of cancers. The DNA is quantitated precisely, *e.g.*, fluorometrically. As a negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (not shown). The 5' nuclease assay (for example, TaqMan™) and real-time quantitative PCR (for example, ABI Prizm 7700 Sequence Detection System™ (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding PRO1295, PRO1293, PRO1265, PRO1303, PRO1269, PRO1410, PRO1317, PRO1780, PRO1555, PRO1755, PRO1558, PRO1759 and PRO1788 is over-represented in any of the primary lung or colon cancers or cancer cell lines or breast cancer cell lines that were screened. The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in Table 7. An explanation of the abbreviations used

for the designation of the primary tumors listed in Table 7 and the primary tumors and cell lines referred to throughout this example has been given hereinbefore.

The results of the TaqMan™ are reported in delta (Δ) Ct units. One unit corresponds to 1 PCR cycle or approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold amplification and so on. Quantitation was obtained using primers and a TaqMan™ fluorescent probe derived from the PRO1295-, PRO1293-, PRO1265-, PRO1303-, PRO1269-, PRO1410-, PRO1317-, PRO1780-, PRO1555-, PRO1755-, PRO1558-, PRO1759- and PRO1788-encoding gene. Regions of PRO1295, PRO1293, PRO1265, PRO1303, PRO1269, PRO1410, PRO1317, PRO1780, PRO1555, PRO1755, PRO1558, PRO1759 and PRO1788 which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced out introns are preferred for the primer and probe derivation, *e.g.*, 3'-untranslated regions. The sequences for the primers and probes (forward, reverse and probe) used for the PRO1295, PRO1293, PRO1265, PRO1303, PRO1269, PRO1410, PRO1317, PRO1780, PRO1555, PRO1755, PRO1558, PRO1759 and PRO1788 gene amplification analysis were as follows:

PRO1295 (DNA59218-1559)

forward: 5'-AGGACTTGCCCTCAGGAA-3' (SEQ ID NO:432)

reverse: 5'-CGCAGGACAGTTGTGAAAATA-3' (SEQ ID NO:433)

probe: 5'-ATGACGCTCGTCCAAGGCCAC-3' (SEQ ID NO:434)

PRO1293 (DNA60618-1557)

forward: 5'-CCCACCTGTACCACCATGT-3' (SEQ ID NO:435)

probe: 5'-ACTCCAGGCACCATCTGTTCTCCC-3' (SEQ ID NO:436)

reverse: 5'-AAGGGCTGGCATTCAAGTU-3' (SEQ ID NO:437)

PRO1265 (DNA60764-1533)

forward: 5'-TGACCTGGCAAAGGAAGAA-3' (SEQ ID NO:438)

probe: 5'-CAGCCACCCTCCAGTCCAAGG-3' (SEQ ID NO:439)

reverse: 5'-GGGTCGTGTTTTGGAGAGA-3' (SEQ ID NO:440)

PRO1303 (DNA65409-1566)

forward: 5'-CTGGCCCTCAGAGCACCAAT-3' (SEQ ID NO:441)

probe: 5'-TCCTCCATCACTTCCCCTAGCTCCA-3' (SEQ ID NO:442)

reverse: 5'-CTGGCAGGAGTTAAAGTTCCAAGA-3' (SEQ ID NO:443)

PRO1269 (DNA66520-1536)

forward: 5'-AAAGGACACCGGGATGTG-3' (SEQ ID NO:444)

probe: 5'-AGCGTACACTCTCTCCAGGCAACCAG-3' (SEQ ID NO:445)

reverse: 5'-CAATTCTGGATGAGGTGGTAGA-3' (SEQ ID NO:446)

PRO1410 (DNA68874-1622)

forward: 5'-CAGGACTGAGCGCTTGTTTA-3' (SEQ ID NO:447)

probe: 5'-CAAAGCGCCAAGTACCGGACC-3' (SEQ ID NO:448)

reverse: 5'-CCAGACCTCAGCCAGGAA-3' (SEQ ID NO:449)

PRO1317 (DNA71166-1685)

forward: 5'-CCCTAGCTGACCCCTTCA-3' (SEQ ID NO:450)

reverse: 5'-TCTGACAAGCAGTTTTCTGAATC-3' (SEQ ID NO:451)

probe: 5'-CTCTCCCCCTCCCTTTTCCTTTGTTT-3' (SEQ ID NO:452)

PRO1780 (DNA71169-1709)

forward: 5'-CTCTGGTGCCCACAGTGA-3' (SEQ ID NO:453)

probe: 5'-CCATGCCTGCTCAGCCAAGAA-3' (SEQ ID NO:454)

reverse: 5'-CAGGAAATCTGGAAACCTACAGT-3' (SEQ ID NO:455)

PRO1555 (DNA73744-1665)

forward: 5'-CCTTGAAAAGGACCCAGTTT-3' (SEQ ID NO:456)

probe: 5'-ATGAGTCGCACCTGCTGTTCCC-3' (SEQ ID NO:457)

reverse: 5'-TAGCAGCTGCCCTTGGTA-3' (SEQ ID NO:458)

forward: 5'-AACAGCAGGTGCGACTCATCTA-3' (SEQ ID NO:459)

probe: 5'-TGCTAGGCGACGACACCCAGACC-3' (SEQ ID NO:460)

reverse: 5'-TGGACACGTGGCAGTGGA-3' (SEQ ID NO:461)

PRO1755 (DNA76396-1698)

forward: 5'-TCATGGTCTCGTCCCATTC-3' (SEQ ID NO:462)

probe: 5'-CACCATTTGTTTCTCTGTCTCCCCATC-3' (SEQ ID NO:463)

reverse: 5'-CCGGCATCCTTGGAGTAG-3' (SEQ ID NO:464)

PRO1788 (DNA77652-2505)

forward: 5'-TCCCCATTAGCACAGGAGTA-3' (SEQ ID NO:465)

probe: 5'-AGGCTCTTGCCTGTCCTGCTGCT-3' (SEQ ID NO:466)

reverse: 5'-GCCCAGAGTCCCACTTGT-3' (SEQ ID NO:467)

PRO1558 (DNA71282-1668)

forward: 5'-ACTGCTCCGCCTACTACGA -3' (SEQ ID NO:468)

probe: 5'-AGGCATCCTCGCCGTCCTCA -3' (SEQ ID NO:469)

reverse: 5'-AAGGCCAAGGTGAGTCCAT -3' (SEQ ID NO:470)

forward: 5'-CGAGTGTGTGCGAAACCTAA -3' (SEQ ID NO:471)

probe: 5'-TCAGGGTCTACATCAGCCTCCTGC -3' (SEQ ID NO:472)

reverse: 5'-AAGGCCAAGGTGAGTCCAT -3' (SEQ ID NO:473)

PRO1759 (DNA76531-1701)

forward: 5'-CCTACTGAGGAGCCCTATGC -3' (SEQ ID NO:474)

probe: 5'-CCTGAGCTGTAACCCCACTCCAGG -3' (SEQ ID NO:231)

reverse: 5'-AGAGTCTGTCCCAGCTATCTTGT -3' (SEQ ID NO:232)

The 5' nuclease assay reaction is a fluorescent PCR-based technique which makes use of the 5' exonuclease activity of Taq DNA polymerase enzyme to monitor amplification in real time. Two oligonucleotide primers are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe, is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when the two dyes are located close together as they are on the probe. During the amplification reaction, the Taq DNA polymerase enzyme cleaves the probe in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the second fluorophore.

One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.

The 5' nuclease procedure is run on a real-time quantitative PCR device such as the ABI Prism 7700TM Sequence Detection. The system consists of a thermocycler, laser, charge-coupled device (CCD) camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

5' Nuclease assay data are initially expressed as Ct, or the threshold cycle. This is defined as the cycle at which the reporter signal accumulates above the background level of fluorescence. The ΔCt values are used as quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample when comparing cancer DNA results to normal human DNA results.

Table 7 describes the stage, T stage and N stage of various primary tumors which were used to screen the PRO1295, PRO1293, PRO1265, PRO1303, PRO1269, PRO1410, PRO1317, PRO1780, PRO1555, PRO1755, PRO1558, PRO1759 and PRO1788 compounds of the invention.

Table 7
Primary Lung and Colon Tumor Profiles

Primary Tumor	Stage	Other Stage	Dukes Stage	T Stage	N Stage
Human lung tumor AdenoCa (SRCC724) [LT1]	IIA			T1	N1
Human lung tumor SqCCa (SRCC725) [LT1a]	IIB			T3	N0
Human lung tumor AdenoCa (SRCC726) [LT2]	IB			T2	N0
Human lung tumor AdenoCa (SRCC727) [LT3]	IIIA			T1	N2
Human lung tumor AdenoCa (SRCC728) [LT4]	IB			T2	N0
Human lung tumor SqCCa (SRCC729) [LT6]	IB			T2	N0
Human lung tumor Aden/SqCCa (SRCC730) [LT7]	IA			T1	N0
Human lung tumor AdenoCa (SRCC731) [LT9]	IB			T2	N0
Human lung tumor SqCCa (SRCC732) [LT10]	IIB			T2	N1
Human lung tumor SqCCa (SRCC733) [LT11]	IIA			T1	N1
Human lung tumor AdenoCa (SRCC734) [LT12]	IV			T2	N0
Human lung tumor AdenoSqCCa (SRCC735)[LT13]	IB			T2	N0
Human lung tumor SqCCa (SRCC736) [LT15]	IB			T2	N0
Human lung tumor SqCCa (SRCC737) [LT16]	IB			T2	N0
Human lung tumor SqCCa (SRCC738) [LT17]	IIB			T2	N1
Human lung tumor SqCCa (SRCC739) [LT18]	IB			T2	N0
Human lung tumor SqCCa (SRCC740) [LT19]	IB			T2	N0
Human lung tumor LCCa (SRCC741) [LT21]	IIB			T3	N1
Human lung AdenoCa (SRCC811) [LT22]	1A			T1	N0
Human colon AdenoCa (SRCC742) [CT2]		M1	D	pT4	N0
Human colon AdenoCa (SRCC743) [CT3]			B	pT3	N0
Human colon AdenoCa (SRCC 744) [CT8]			B	T3	N0
Human colon AdenoCa (SRCC745) [CT10]		A	pT2	N0	
Human colon AdenoCa (SRCC746) [CT12]	MO, R1	B	T3	N0	
Human colon AdenoCa (SRCC747) [CT14]	pMO, RO	B	pT3	pN0	
Human colon AdenoCa (SRCC748) [CT15]	M1, R2	D	T4	N2	
Human colon AdenoCa (SRCC749) [CT16]	pMO	B	pT3	pN0	
Human colon AdenoCa (SRCC750) [CT17]		C1	pT3	pN1	
Human colon AdenoCa (SRCC751) [CT1]		MO, R1	B	pT3	N0
Human colon AdenoCa (SRCC752) [CT4]			B	pT3	M0
Human colon AdenoCa (SRCC753) [CT5]		G2	C1	pT3	pN0
Human colon AdenoCa (SRCC754) [CT6]		pMO, RO	B	pT3	pN0
Human colon AdenoCa (SRCC755) [CT7]		G1	A	pT2	pN0
Human colon AdenoCa (SRCC756) [CT9]		G3	D	pT4	pN2
Human colon AdenoCa (SRCC757) [CT11]		B	T3	N0	
Human colon AdenoCa (SRCC758) [CT18]	MO, RO	B	pT3	pN0	

DNA Preparation:

DNA was prepared from cultured cell lines, primary tumors, and normal human blood. The isolation was performed using purification kit, buffer set and protease and all from Qiagen, according to the manufacturer's instructions and the description below.

Cell culture lysis:

Cells were washed and trypsinized at a concentration of 7.5×10^8 per tip and pelleted by centrifuging at 1000 rpm for 5 minutes at 4°C, followed by washing again with 1/2 volume of PBS and recentrifugation. The pellets were washed a third time, the suspended cells collected and washed 2x with PBS. The cells were then suspended into 10 ml PBS. Buffer C1 was equilibrated at 4°C. Qiagen protease #19155 was diluted into 6.25 ml cold ddH_20 to a final concentration of 20 mg/ml and equilibrated at 4°C. 10 ml of G2 Buffer was prepared by diluting Qiagen RNAse A stock (100 mg/ml) to a final concentration of 200 μg/ml.

Buffer C1 (10 ml, 4°C) and ddH2O (40 ml, 4°C) were then added to the 10 ml of cell suspension, mixed by inverting and incubated on ice for 10 minutes. The cell nuclei were pelleted by centrifuging in a Beckman swinging bucket rotor at 2500 rpm at 4°C for 15 minutes. The supernatant was discarded and the nuclei were suspended with a vortex into 2 ml Buffer C1 (at 4°C) and 6 ml ddH_2O, followed by a second 4°C centrifugation at 2500 rpm for 15 minutes. The nuclei were then resuspended into the residual buffer using 200 μl per tip. G2 buffer (10 ml) was added to the suspended nuclei while gentle vortexing was applied. Upon completion of buffer addition, vigorous vortexing was applied for 30 seconds. Quiagen protease (200 μl, prepared as indicated above) was added and incubated at 50°C for 60 minutes. The incubation and centrifugation were repeated until the lysates were clear (*e.g.*, incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

Solid human tumor sample preparation and lysis:

Tumor samples were weighed and placed into 50 ml conical tubes and held on ice. Processing was limited to no more than 250 mg tissue per preparation (1 tip/preparation). The protease solution was freshly prepared by diluting into 6.25 ml cold ddH_2O to a final concentration of 20 mg/ml and stored at 4°C. G2 buffer (20 ml) was prepared by diluting DNAse A to a final concentration of 200 mg/ml (from 100 mg/ml stock). The tumor tissue was homogenated in 19 ml G2 buffer for 60 seconds using the large tip of the polytron in a laminar-flow TC hood in order to avoid inhalation of aerosols, and held at room temperature. Between samples, the polytron was cleaned by spinning at 2 x 30 seconds each in 2L ddH_20, followed by G2 buffer (50 ml). If tissue was still present on the generator tip, the apparatus was disassembled and cleaned.

Quiagen protease (prepared as indicated above, 1.0 ml) was added, followed by vortexing and incubation at 50°C for 3 hours. The incubation and centrifugation were repeated until the lysates were clear (*e.g.*, incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

Human blood preparation and lysis:

Blood was drawn from healthy volunteers using standard infectious agent protocols and citrated into 10 ml samples per tip. Quiagen protease was freshly prepared by dilution into 6.25 ml cold ddH_2O to a final concentration of 20 mg/ml and stored at 4°C. G2 buffer was prepared by diluting RNAse A to a final concentration of 200 μg/ml from 100 mg/ml stock. The blood (10 ml) was placed into a 50 ml conical tube and 10 ml C1 buffer and 30 ml ddH_2O (both previously equilibrated to 4°C) were added, and the components mixed by inverting and held on ice for 10 minutes. The nuclei were pelleted with a Beckman swinging bucket rotor at 2500 rpm, 4°C for 15 minutes and the supernatant discarded. With a vortex, the nuclei were suspended into 2 ml C1 buffer (4°C) and 6 ml ddH_2O (4°C). Vortexing was repeated until the pellet was white. The nuclei were then suspended into the residual buffer using a 200 μl tip. G2 buffer (10 ml) was added to the suspended nuclei while gently vortexing, followed by vigorous vortexing for 30 seconds. Quiagen protease was added (200 μl) and incubated at 50°C for 60 minutes. The incubation and centrifugation were repeated until the lysates were clear (*e.g.*, incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

Purification of cleared lysates:

(1) <u>Isolation of genomic DNA</u>:

Genomic DNA was equilibrated (1 sample per maxi tip preparation) with 10 ml QBT buffer. QF elution buffer was equilibrated at 50°C. The samples were vortexed for 30 seconds, then loaded onto equilibrated tips and drained by gravity. The tips were washed with 2 x 15 ml QC buffer. The DNA was eluted into 30 ml silanized, autoclaved 30 ml Corex tubes with 15 ml QF buffer (50°C). Isopropanol (10.5 ml) was added to each

sample, the tubes covered with parafin and mixed by repeated inversion until the DNA precipitated. Samples were pelleted by centrifugation in the SS-34 rotor at 15,000 rpm for 10 minutes at 4°C. The pellet location was marked, the supernatant discarded, and 10 ml 70% ethanol (4°C) was added. Samples were pelleted again by centrifugation on the SS-34 rotor at 10,000 rpm for 10 minutes at 4°C. The pellet location was marked and the supernatant discarded. The tubes were then placed on their side in a drying rack and dried 10 minutes at 37°C, taking care not to overdry the samples.

After drying, the pellets were dissolved into 1.0 ml TE (pH 8.5) and placed at 50°C for 1-2 hours. Samples were held overnight at 4°C as dissolution continued. The DNA solution was then transferred to 1.5 ml tubes with a 26 gauge needle on a tuberculin syringe. The transfer was repeated 5x in order to shear the DNA. Samples were then placed at 50°C for 1-2 hours.

(2) Quantitation of genomic DNA and preparation for gene amplification assay:

The DNA levels in each tube were quantified by standard A_{260}/ A_{280} spectrophotometry on a 1:20 dilution (5 μl DNA + 95 μl ddH_2O) using the 0.1 ml quartz cuvettes in the Beckman DU640 spectrophotometer. A_{260}/A_{280} ratios were in the range of 1.8-1.9. Each DNA sample was then diluted further to approximately 200 ng/ml in TE (pH 8.5). If the original material was highly concentrated (about 700 ng/μl), the material was placed at 50°C for several hours until resuspended.

Fluorometric DNA quantitation was then performed on the diluted material (20-600 ng/ml) using the manufacturer's guidelines as modified below. This was accomplished by allowing a Hoeffer DyNA Quant 200 fluorometer to warm-up for about 15 minutes. The Hoechst dye working solution (#H33258, 10 μl, prepared within 12 hours of use) was diluted into 100 ml 1 x TNE buffer. A 2 ml cuvette was filled with the fluorometer solution, placed into the machine, and the machine was zeroed. pGEM 3Zf(+) (2 μl, lot #360851026) was added to 2 ml of fluorometer solution and calibrated at 200 units. An additional 2 μl of pGEM 3Zf(+) DNA was then tested and the reading confirmed at 400 +/- 10 units. Each sample was then read at least in triplicate. When 3 samples were found to be within 10% of each other, their average was taken and this value was used as the quantification value.

The fluorometricly determined concentration was then used to dilute each sample to 10 ng/μl in ddH_2O. This was done simultaneously on all template samples for a single TaqMan plate assay, and with enough material to run 500-1000 assays. The samples were tested in triplicate with Taqman™ primers and probe both B-actin and GAPDH on a single plate with normal human DNA and no-template controls. The diluted samples were used provided that the CT value of normal human DNA subtracted from test DNA was +/- 1 Ct. The diluted, lot-qualified genomic DNA was stored in 1.0 ml aliquots at -80°C. Aliquots which were subsequently to be used in the gene amplification assay were stored at 4°C. Each 1 ml aliquot is enough for 8-9 plates or 64 tests.

Gene amplification assay:

The PRO1295, PRO1293, PRO1265, PRO1303, PRO1269, PRO1410, PRO1317, PRO1780, PRO1555, PRO1755, PRO1558, PRO1759 and PRO1788 compounds of the invention were screened in the following primary tumors and the resulting ΔCt values which are ≥1.0 are reported in Table 8.

Table 8

ΔCt values in lung and colon primary tumors and cell line models

Primary Tumors or Cell lines	PRO 1293	PRO 1269	PRO 1410	PRO 1755	PRO 1780	PRO 1788	PRO 1303	PRO 1555	PRO 1265	PRO 1317	PRO 1295	PRO 1558	PRO 1759
LT1	---	---	---	---	---	---	---	---	---	1.15	---	---	---
LT1-a	---	---	---	---	---	---	---	---	---	1.49	---	---	---
LT3	---	---	---	---	---	---	---	---	1.04	---	---	---	---
LT4	---	---	---	---	1.16	---	---	---	---	---	---	---	---
LT7	---	---	---	---	1.02	---	---	---	---	---	---	---	---
LT9	---	---	---	---	---	---	---	---	---	1.26	---	---	---
LT10	---	---	---	---	---	---	---	---	---	1.68	---	---	---
LT12	---	---	---	---	---	---	---	---	2.17	---	---	---	---
LT13	---	---	1.12 1.42	---	---	---	1.42	4.20 4.45	2.24	---	---	---	---
LT15	---	1.22	2.10 1.82	---	---	---	1.17	1.36 1.15	3.51	1.16	---	---	---
LT16	---	1.14	1.44 1.45	1.36	---	---	1.42	3.71 3.99	3.32	---	---	---	---
LT17	---	1.26	---	---	---	---	---	---	1.02	1.74	---	---	---
LT18	---	---	---	1.18	---	---	---	---	---	---	---	---	---
CT2	---	---	2.36	2.35	---	---	---	---	---	---	---	---	---
CT3	---	---	1.09	---	---	1.35	---	---	---	---	---	---	---
CT8	---	---	---	1.64	---	1.26	---	---	---	---	---	---	---
CT10	---	---	1.41	2.05	---	1.37	---	---	---	---	---	---	---
CT12	---	---	---	1.15	---	1.24	---	---	---	---	---	---	---
CT14	---	---	1.46	1.40	---	2.58	---	---	---	---	---	---	---
CT15	---	---	---	---	---	---	---	1.34 1.62	---	---	---	---	---
CT16	---	---	---	---	---	---	1.13	1.04 1.05	---	---	---	---	---
CT17	---	---	---	---	---	---	---	1.16	---	---	---	---	---
CT1	---	---	---	---	---	1.09	---	---	---	---	---	---	---
CT4	---	---	---	---	---	1.22	---	---	---	---	---	---	---
CT5	---	---	2.14	---	---	---	---	---	---	---	---	---	---
CT9	---	---	---	---	---	1.52	---	---	---	---	---	---	---
CT11	---	---	1.29	---	---	---	---	---	---	---	---	---	---
A549	---	---	---	---	---	---	1.20	2.17 2.11	---	---	---	---	---

Calu-1	---	---	---	---	---	---	---	1.39	---	---	---	---	---
Calu-6	---	---	---	---	---	---	---	1.12	---	---	---	---	---
H441	---	---	---	---	---	---	---	2.06	---	---	---	---	---
H460	---	---	---	---	---	---	---	1.88	---	---	---	---	---
SKMES 1	---	---	---	---	---	---	---	1.90	---	---	---	---	---
SW620	---	---	---	---	---	---	---	2.24	---	---	---	---	---
Colo320	---	---	---	---	---	---	---	2.21 2.24	---	---	---	---	---
HT29	---	---	1.22	---	---	---	---	---	---	---	---	---	---
HCT116	---	---	---	---	---	---	---	2.46 2.66	---	---	---	---	---
LT22	---	---	---	1.26	1.07	---	---	---	---	2.69	---	---	---
HF-000716	---	---	---	---	---	---	---	2.63 2.73	---	---	---	---	---
HF-000733	---	---	---	---	---	---	---	2.58 2.71 1.39	---	---	---	---	---
HF-000611	---	---	---	---	---	---	---	4.99	---	---	---	---	---
HF-000539	2.33	---	---	---	---	---	---	3.13 2.55	---	---	1.49	---	---
HF-000575	---	---	---	---	---	---	---	1.32	---	---	---	---	---
HF-000698	---	---	---	---	---	---	---	---	---	---	1.09	---	---
HF-000545	---	---	---	---	---	---	---	1.59 1.68	---	---	1.11	---	---
HF-000631	---	---	---	---	---	---	---	1.37	---	---	1.27	---	---
HF-000840	1.71	---	---	---	---	---	---	3.63	---	---	1.97	1.39	1.11
HF-000842	---	---	---	---	---	---	---	1.99	---	---	---	1.24	---
HF-000795	1.13	---	---	---	---	---	---	---	---	---	---	1.01	1.32
HF-001294	---	---	---	---	---	---	---	---	---	---	---	1.50	---
HF-001296	---	---	---	---	---	---	---	---	---	---	---	2.88	1.51
HF-001299	---	---	---	---	---	---	---	---	---	---	---	1.37	---

PRO1265

PRO1265 (DNA60764-1533) was also reexamined along with selected tumors from the above initial screen with framework mapping. Table 9 indicates the chromosomal mapping of the framework markers that were used in the present example. The framework markers are located approximately every 20 megabases and were used to control aneuploidy.

PRO1265 was also reexamined with epicenter mapping. The markers indicated in Table 10 are located in close proximity (in the genome) to DNA60764-1533, and are used to assess the relative amplification in the immediate vicinity of Chromosome 19 wherein the molecule is located. The distance between individual markers is measured in centirays (cR), which is a radiation breakage unit approximately equal to a 1% chance of a breakage between two markers. One cR is very roughly equivalent to 20 kilobases. The marker SHGC-33698 is closest to DNA60764-1533.

Table 9
Framework Markers Along Chromosome 19

Map Position on Chromosome 19	Stanford Human Genome Center Marker Name
S12	AFMa107xc9
S50	SHGC-31335
S105	SHGC-34102
S155	SHGC-16175

Table 10
Epicenter Markers Along Chromosome 19 used for DNA60764-1533

Map Position on Chromosome 19	Stanford Human Genome Center Marker Name	Distance to next Marker (cR)
DNA34353	—	maps to S158
DNA40620	—	maps to S160
DNA54002	—	maps to S160
S160	SHGC-34723	21
DNA60764	—	—
S161	SHGC-30929	15
S162	SHGC-10328	17
S163	AFMa115wg5	—

The ΔCt values of the above described framework markers along Chromosome 19 relative to PRO1265 are indicated for selected tumors in Table 11.

Table 11

Amplification of framework markers relative to DNA60764-1533 (ΔCt)

Tumor	Framework Markers				
	S12	DNA60764-1533	S50	S105	S155
LT1	0.16	0.06	-0.42	0.11	-1.56
LT1a	0.05	-0.27	0.17	0.40	0.00
LT2	0.48	0.41	0.52	0.13	-0.36
LT3	0.27	0.83	0.11	0.50	1.04
LT4	0.48	0.67	0.20	0.56	-0.35
LT6	0.72	0.74	0.32	0.35	0.24
LT7	0.82	0.85	0.95	0.95	0.75
LT9	0.72	0.61	0.19	0.64	-0.35
LT10	0.82	0.98	0.62	0.53	0.32
LT11	0.13	0.25	0.55	-0.34	0.70
LT12	0.04	0.60	0.21	-0.17	2.17
LT13	-0.06	0.57	-0.30	-0.05	2.24
LT15	-0.03	-0.77	0.12	-0.04	3.51
LT16	0.46	1.37	0.51	0.23	3.32
LT17	0.37	0.74	0.21	0.22	1.02
LT18	0.39	0.57	0.11	0.16	0.52
LT22	0.79	0.76	-0.05	0.16	0.59

DISCUSSION AND CONCLUSION:

PRO1269 (DNA66520-1536):

The ΔCt values for DNA66520-1536 in a variety of tumors are reported above. A ΔCt of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. The above data indicates that significant amplification of nucleic acid DNA66520-1536 encoding PRO1269 occurred in primary lung tumors: LT15, LT16 and LT17. Because amplification of DNA66520-1536 occurs in various lung tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA66520-1536 (PRO1269) would be expected to have utility in cancer therapy.

PRO1410 (DNA68874-1622):

The ΔCt values for DNA68874-1622 in a variety of tumors are reported above. A ΔCt of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. the

above data indicates that significant amplification of nucleic acid DNA68874-1622 encoding PRO1410 occurred: (1) in primary lung tumors: LT13, LT15 and LT16; (2) in primary colon tumors: CT2, CT3, CT5, CT10, CT11, and CT14; and (3) in colon cell line HT29. Because amplification of DNA68874-1622 occurs in various lung and colon tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA68874-1622 (PRO1410) would be expected to have utility in cancer therapy.

PRO1755 (DNA76396-1698):

The ΔCt values for DNA76396-1698 in a variety of tumors are reported above. A ΔCt of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. The above data indicates that significant amplification of nucleic acid DNA76396-1698 encoding PRO1755 occurred: (1) in primary lung tumors: LT16, LT18 and LT22; and (2) in primary colon tumors: CT2, CT8, CT10, CT12, and CT14. Because amplification of DNA76396-1698 occurs in various lung and colon tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA76396-1698 (PRO1755) would be expected to have utility in cancer therapy.

PRO1780 (DNA71169-1709):

The ΔCt values for DNA71169-1709 in a variety of tumors are reported above. A ΔCt of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. The above data indicates that significant amplification of nucleic acid DNA71169-1709 encoding PRO1780 occurred in primary lung tumors: LT4, LT7 and LT22. Because amplification of DNA71169-1709 occurs in various lung tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA71169-1709 (PRO1780) would be expected to have utility in cancer therapy.

PRO1788 (DNA77652-2505):

The ΔCt values for DNA77652-2505 in a variety of tumors are reported above. A ΔCt of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. The above data indicates that significant amplification of nucleic acid DNA77652-2505 encoding PRO1788 occurred in primary colon tumors: CT1, CT3, CT4, CT8, CT9, CT10, CT12, and CT14. Because amplification of DNA77652-2505 occurs in various colon tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA77652-2505 (PRO1788) would be expected to have utility in cancer therapy.

PRO1295 (DNA59218-1559):

The ΔCt values for DNA59218-1559 in a variety of tumors are reported above. A ΔCt of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. The above data indicates that significant amplification of nucleic acid DNA59218-1559 encoding PRO1295 occurred: (1) in primary lung tumors: HF-000631 and HF-000840; (2) colon tumor centers: HF-000539 and HF-000698;

and (3) in breast tumor center HF-000545. Because amplification of DNA59218-1559 occurs in various tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA59218-1559 (PRO1295) would be expected to have utility in cancer therapy.

PRO1293 (DNA60618-1557):

The ΔCt values for DNA60618-1557 in a variety of tumors are reported above. A ΔCt of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. The above data indicates that significant amplification of nucleic acid DNA60618-1557 encoding PRO1293 occurred: (1) in primary lung tumor HF-000840; and (2) in colon tumor centers: HF-000539 and HF-000795. Because amplification of DNA60618-1557 occurs in various lung and colon tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA60618-1557 (PRO1293) would be expected to have utility in cancer therapy.

PRO1303 (DNA65409-1566):

The ΔCt values for DNA65409-1566 in a variety of tumors are reported above. A ΔCt of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. The above data indicates that significant amplification of nucleic acid DNA65409-1566 encoding PRO1303 occurred: (1) in primary lung tumors: LT13, LT15 and LT16; (2) in lung cell line A549; and (3) in colon tumor CT16. Because amplification of DNA65409-1566 occurs in various tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA65409-1566 (PRO1566) would be expected to have utility in cancer therapy.

PRO1555 (DNA73744-1665):

The ΔCt values for DNA73744-1665 in a variety of tumors are reported above. A ΔCt of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. The above data indicates that significant amplification of nucleic acid DNA73744-1665 encoding PRO1555 occurred: (1) in primary lung tumors: LT13, LT15, LT16, HF-000631, HF-000840, and HF-000842; (2) in lung cell lines: A549, Calu-1, Calu-6, H441, H460, and SKMES1; (3) in primary colon tumors: CT15, CT16, CT17, and colon tumor centers HF-000539 and HF-000575; (4) in colon cell lines: SW620, Colo320 and HCT116; (5) in breast tumor center HF-000545; (6) in kidney tumor center HF-000611; and (7) in testis tumor margin HF-000716 and testis tumor center HF-000733. Because amplification of DNA73744-1665 occurs in various tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA73744-1665 (PRO1555) would be expected to have utility in cancer therapy.

PRO1265 (DNA60764-1533):

The ΔCt values for DNA60764-1533 in a variety of lung tumors are reported above. A ΔCt value of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. The above data indicates that significant amplification of DNA60765-1533 occurred in primary lung

tumors LT3, LT12, LT13, LT15, LT16 and LT17. The ΔCt values of these hits are 1.03, 2.17, 2.24, 3.51, 3.32 and 1.02. This represents an increase in gene copy of approximately 2.04, 4.50, 4.72, 11.39, 9.99 and 2.03.

Amplification has also been confirmed framework mapping for DNA60764-1533 in LT16. The reported ΔCt value was 1.37, which represents a 2.58 fold increase in gene copy relative to normal tissue. Epicenter mapping has also confirmed amplification of DNA60764-1533 in LT12, LT13, LT15, LT16, CT1, CT4, CT5, CT7 and CT11. These tumors report ΔCt values of 2.35, 2.37, 3.88, 3.32 in the lung tumors and 1.74, 1.86, 3.28, 1.29 and 2.32 in the colon tumors. Relative to normal tissue, this represents an increase in gene copy of approximately 5.10, 5.17, 14.72 and 9.98 in the lung tumors and 3.34, 3.63, 9.71, 2.45 and 4.99 in the colon tumors.

In contrast, the amplification of the closest known framework markers, epicenter markers and the comparison sequences does not occur to a greater extent than that of DNA60764-1533. This strongly suggests that DNA60764-1533 is the gene responsible for the amplification of the particular region in Chromosome 19. Because amplification of DNA60764-1533 occurs in various lung and colon tumors, it is highly probably to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA60764-1533 would be expected to have utility in cancer therapy.

PRO1317 (DNA71166-1685):

The ΔCt values for DNA71166-1685 in a variety of tumors are reported above. A ΔCt of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. The above data indicates that significant amplification of nucleic acid DNA71166-1685 encoding PRO1317 occurred in primary lung tumors LT1, LT1a, LT9, LT10, LT15, LT17 and LT22 . Because amplification of DNA71166-1685 occurs in various tumors, it is likely associated with tumor formation and/or growth. As a result, antagonists (*e.g.*, antibodies) directed against PRO1317 would be expected to be useful in cancer therapy.

Summary

Because amplification of the various DNA's as described above occurs in various tumors, they are likely associated with tumor formation and/or growth. As a result, antagonists (*e.g.*, antibodies) directed against these polypeptides would be expected to be useful in cancer therapy.

EXAMPLE 144: Stimulatory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 24)

This example shows that certain polypeptides of the invention are active as a stimulator of the proliferation of stimulated T-lymphocytes. Compounds which stimulate proliferation of lymphocytes are useful therapeutically where enhancement of an immune response is beneficial. A therapeutic agent may take the form of antagonists of the polypeptide of the invention, for example, murine-human chimeric, humanized or human antibodies against the polypeptide.

The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Insitutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO_2) and then washed and resuspended to $3x10^6$ cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:l of test sample diluted to 1% or to 0.1%,

50 :l of irradiated stimulator cells, and

50 :l of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO_2 for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mC/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to $1x10^7$ cells/ml of assay media. The assay is then conducted as described above.

Positive increases over control are considered positive with increases of greater than or equal to 180% being preferred. However, any value greater than control indicates a stimulatory effect for the test protein.

The following PRO polypeptides tested positive in this assay: PRO1246 and PRO1343.

EXAMPLE 145: Mouse Kidney Mesangial Cell Proliferation Assay (Assay 92)

This assay shows that certain polypeptides of the invention act to induce proliferation of mammalian kidney mesangial cells and, therefore, are useful for treating kidney disorders associated with decreased mesangial cell function such as Berger disease or other nephropathies associated with Schönlein-Henoch purpura, celiac disease, dermatitis herpetiformis or Crohn disease. The assay is performed as follows. On day one, mouse kidney mesangial cells are plated on a 96 well plate in growth media (3:1 mixture of Dulbecco's modified Eagle's medium and Ham's F12 medium, 95% fetal bovine serum, 5% supplemented with 14 mM HEPES) and grown overnight. On day 2, PRO polypeptides are diluted at 2 concentrations(1% and 0.1%) in serum-free medium and added to the cells. Control samples are serum-free medium alone. On day 4, 20μl of the Cell Titer 96 Aqueous one solution reagent (Progema) was added to each well and the colormetric reaction was allowed to proceed for 2 hours. The absorbance (OD) is then measured at 490 nm. A positive in the assay is anything that gives an absorbance reading which is at least 15% above the control reading.

The following polypeptide tested positive in this assay: PRO1265, PRO1244 and PRO1382.

EXAMPLE 146: Induction of Pancreatic β-Cell Precursor Differentiation (Assay 89)

This assay shows that certain polypeptides of the invention act to induce differentiation of pancreatic

β-cell precursor cells into mature pancreatic β-cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent either β-cell precursors or mature β-cells. Marker expression is measured by real time quantitative PCR (RTQ-PCR); wherein the marker being evaluated is insulin.

The pancreata are dissected from E14 embryos (CD1 mice). The pancreata are then digested with collagenase/dispase in F12/DMEM at 37°C for 40 to 60 minutes (collagenase/dispase, 1.37 mg/ml, Boehringer Mannheim, #1097113). The digestion is then neutralized with an equal volume of 5% BSA and the cells are washed once with RPMI1640. At day 1, the cells are seeded into 12-well tissue culture plates (pre-coated with laminin, 20μg/ml in PBS, Boehringer Mannheim, #124317). Cells from pancreata from 1-2 embryos are distributed per well. The culture medium for this primary cuture is 14F/1640. At day 2, the media is removed and the attached cells washed with RPMI/1640. Two mls of minimal media are added in addition to the protein to be tested. At day 4, the media is removed and RNA prepared from the cells and marker expression analyzed by real time quantitative RT-PCR. A protein is considered to be active in the assay if it increases the expression of the relevant β-cell marker as compared to untreated controls.

14F/1640 is RPMI1640 (Gibco) plus the following:

group A 1:1000

group B 1:1000

recombinant human insulin 10 μg/ml

Aprotinin (50μg/ml) 1:2000 (Boehringer manheim #981532)

Bovine pituitary extract (BPE) 60μg/ml

Gentamycin 100 ng/ml

Group A : (in 10ml PBS)

Transferrin, 100mg (Sigma T2252)

Epidermal Growth Factor, 100μg (BRL 100004)

Triiodothyronine, 10μl of $5x10^{-6}$ M (Sigma T5516)

Ethanolamine, 100μl of 10^{-1} M (Sigma E0135)

Phosphoethalamine, 100μl of 10^{-1} M (Sigma P0503)

Selenium, 4μl of 10^{-1} M (Aesar #12574)

Group C : (in 10ml 100% ethanol)

Hydrocortisone, 2μl of $5X10^{-3}$ M (Sigma #H0135)

Progesterone, 100μl of $1X10^{-3}$ M (Sigma #P6149)

Forskolin, 500μl of 20mM (Calbiochem #344270)

Minimal media:

RPMI 1640 plus transferrin (10 μg/ml), insulin (1 μg/ml), gentamycin (100 ng/ml), aprotinin (50 μg/ml) and BPE (15 μg/ml).

Defined media:

RPMI 1640 plus transferrin (10 μg/ml), insulin (1 μg/ml), gentamycin (100 ng/ml) and aprotinin (50 μg/ml).

The following polypeptides were positive in this assay: PRO1275 and PRO1474.

EXAMPLE 147: Fetal Hemoglobin Induction in an Erythroblastic Cell Line (Assay 107)

This assay is useful for screening PRO polypeptides for the ability to induce the switch from adult hemoglobin to fetal hemoglobin in an erythroblastic cell line. Molecules testing positive in this assay are expected to be useful for therapeutically treating various mammalian hemoglobin-associated disorders such as the various thalassemias. The assay is performed as follows. Erythroblastic cells are plated in standard growth medium at 1000 cells/well in a 96 well format. PRO polypeptides are added to the growth medium at a concentration of 0.2% or 2% and the cells are incubated for 5 days at 37°C. As a positive control, cells are treated with 100μM hemin and as a negative control, the cells are untreated. After 5 days, cell lysates are prepared and analyzed for the expression of gamma globin (a fetal marker). A positive in the assay is a gamma globin level at least 2-fold above the negative control.

The following polypeptides tested positive in this assay: PRO1478, PRO1265, PRO1412, PRO1279, PRO1304, PRO1306, PRO1418, PRO1410 and PRO1575.

EXAMPLE 148: Detection of Polypeptides That Affect Glucose and/or FFA Uptake in Skeletal Muscle (Assay 106)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by skeletal muscle cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by skeletal muscle would be beneficial including, for example, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat differentiated skeletal muscle, and allowed to incubate overnight. Then fresh media with the PRO polypeptide and +/- insulin are added to the wells. The sample media is then monitored to determine glucose and FFA uptake by the skeletal muscle cells. The insulin will stimulate glucose and FFA uptake by the skeletal muscle, and insulin in media without the PRO polypeptide is used as a positive control, and a limit for scoring. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as either stimulators or inhibitors of glucose and/or FFA uptake in this assay: PRO1130, PRO1275, PRO1418, PRO1555 and PRO1787.

EXAMPLE 149: Detection of PRO Polypeptides That Affect Glucose or FFA Uptake by Primary Rat Adipocytes (Assay 94)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by adipocyte cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and FFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as stimulators of glucose and/or FFA uptake in this assay: PRO1265, PRO1283, PRO1279, PRO1303, PRO1306, PRO1325, PRO1565 and PRO1567.

The following PRO polypeptides tested positive as inhibitors of glucose and/or FFA uptake in this assay: PRO1194, PRO1190, PRO1326, PRO1343, PRO1480, PRO1474, PRO1575 and PRO1760.

EXAMPLE 150: Chondrocyte Re-differentiation Assay (Assay 110)

This assay shows that certain polypeptides of the invention act to induce redifferentiation of chondrocytes, therefore, are expected to be useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. The assay is performed as follows. Porcine chondrocytes are isolated by overnight collagenase digestion of articulary cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm^2 in Ham F-12 containing 10% FBS and 4 μg/ml gentamycin. The culture media is changed every third day and the cells are then seeded in 96 well plates at 5,000 cells/well in 100μl of the same media without serum and 100 μl of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 μl/well. After 5 days of incubation at 37°C, a picture of each well is taken and the differentiation state of the chondrocytes is determined. A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control.

The following polypeptide tested positive in this assay: PRO1265, PRO1250, PRO1430, PRO1356, PRO1275, PRO1274, PRO1286, PRO1273, PRO1283, PRO1279, PRO1306, PRO1325, PRO1343, PRO1418, PRO1565, PRO1474, PRO1787, PRO1556 and PRO1801.

EXAMPLE 151: Induction of Pancreatic β-Cell Precursor Proliferation (Assay 117)

This assay shows that certain polypeptides of the invention act to induce an increase in the number of pancreatic β-cell precursor cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent either β-cell precursors or mature β-cells. Marker expression is measured by real time quantitative PCR (RTQ-PCR); wherein the marker being evaluated is a transcription factor called Pdx1.

The pancreata are dissected from E14 embryos (CD1 mice). The pancreata are then digested with collagenase/dispase in F12/DMEM at 37°C for 40 to 60 minutes (collagenase/dispase, 1.37 mg/ml, Boehringer Mannheim, #1097113). The digestion is then neutralized with an equal volume of 5% BSA and the cells are washed once with RPMI1640. At day 1, the cells are seeded into 12-well tissue culture plates (pre-coated with laminin, 20μg/ml in PBS, Boehringer Mannheim, #124317). Cells from pancreata from 1-2 embryos are

distributed per well. The culture medium for this primary cuture is 14F/1640. At day 2, the media is removed and the attached cells washed with RPMI/1640. Two mls of minimal media are added in addition to the protein to be tested. At day 4, the media is removed and RNA prepared from the cells and marker expression analyzed by real time quantitative RT-PCR. A protein is considered to be active in the assay if it increases the expression of the relevant β-cell marker as compared to untreated controls.

14F/1640 is RPMI1640 (Gibco) plus the following:

group A 1:1000

group B 1:1000

recombinant human insulin 10 μg/ml

Aprotinin (50μg/ml) 1:2000 (Boehringer manheim #981532)

Bovine pituitary extract (BPE) 60μg/ml

Gentamycin 100 ng/ml

Group A : (in 10ml PBS)

Transferrin, 100mg (Sigma T2252)

Epidermal Growth Factor, 100μg (BRL 100004)

Triiodothyronine, 10μl of $5x10^{-6}$ M (Sigma T5516)

Ethanolamine, 100μl of 10^{-1} M (Sigma E0135)

Phosphoethalamine, 100μl of 10^{-1} M (Sigma P0503)

Selenium, 4μl of 10^{-1} M (Aesar #12574)

Group C : (in 10ml 100% ethanol)

Hydrocortisone, 2μl of $5X10^{-3}$ M (Sigma #H0135)

Progesterone, 100μl of $1X10^{-3}$ M (Sigma #P6149)

Forskolin, 500μl of 20mM (Calbiochem #344270)

Minimal media:

RPMI 1640 plus transferrin (10 μg/ml), insulin (1 μg/ml), gentamycin (100 ng/ml), aprotinin (50 μg/ml) and BPE (15 μg/ml).

Defined media:

RPMI 1640 plus transferrin (10 μg/ml), insulin (1 μg/ml), gentamycin (100 ng/ml) and aprotinin (50 μg/ml).

The following polypeptides tested positive in this assay: PRO1382 and PRO1561.

EXAMPLE 152: Proliferation of Rat Utricular Supporting Cells (Assay 54)

This assay shows that certain polypeptides of the invention act as potent mitogens for inner ear supporting cells which are auditory hair cell progenitors and, therefore, are useful for inducing the regeneration of auditory hair cells and treating hearing loss in mammals. The assay is performed as follows. Rat UEC-4 utricular epithelial cells are aliquoted into 96 well plates with a density of 3000 cells/well in 200 μl of serum-containing medium at 33°C. The cells are cultured overnight and are then switched to serum-free medium at 37°C. Various dilutions of PRO polypeptides (or nothing for a control) are then added to the cultures and the cells are incubated for 24 hours. After the 24 hour incubation, ^{3}H-thymidine (1 μCi/well) is added and the cells

are then cultured for an additional 24 hours. The cultures are then washed to remove unincorporated radiolabel, the cells harvested and Cpm per well determined. Cpm of at least 30% or greater in the PRO polypeptide treated cultures as compared to the control cultures is considered a positive in the assay.

The following polypeptides tested positive in this assay: PRO1340.

EXAMPLE 153: Chondrocyte Proliferation Assay (Assay 111)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce the proliferation and/or redifferentiation of chondrocytes in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis.

Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of the metacarpophalangeal joint of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm^2 in Ham F-12 containing 10% FBS and 4 μg/ml gentamycin. The culture media is changed every third day and the cells are reseeded to 25,000 cells/cm^2 every five days. On day 12, the cells are seeded in 96 well plates at 5,000 cells/well in 100μl of the same media without serum and 100 μl of either serum-free medium (negative control), staurosporin (final concentration of 5 nM; positive control) or the test PRO polypeptide are added to give a final volume of 200 μl/well. After 5 days at 37°C, 20 μl of Alamar blue is added to each well and the plates are incubated for an additional 3 hours at 37°C. The fluorescence is then measured in each well (Ex:530 nm; Em: 590 nm). The fluorescence of a plate containing 200 μl of the serum-free medium is measured to obtain the background. A positive result in the assay is obtained when the fluorescence of the PRO polypeptide treated sample is more like that of the positive control than the negative control.

The following PRO polypeptides tested positive in this assay: PRO1265, PRO1412, PRO1347, PRO1279, PRO1410 and PRO1474.

EXAMPLE 154: Inhibition of Heart Neonatal Hypertrophy Induced by LIF+ET-1 (Assay 74)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to inhibit neonatal heart hypertrophy induced by LIF and endothelin-1 (ET-1). A test compound that provides a positive response in the present assay would be useful for the therapeutic treatment of cardiac insufficiency diseases or disorders characterized or associated with an undesired hypertrophy of the cardiac muscle.

Cardiac myocytes from 1-day old Harlan Sprague Dawley rats (180 μl at 7.5 x 10^4/ml, serum <0.1, freshly isolated) are introduced on day 1 to 96-well plates previously coated with DMEM/F12 + 4%FCS. Test PRO polypeptide samples or growth medium alone (negative control) are then added directly to the wells on day 2 in 20 μl volume. LIF + ET-1 are then added to the wells on day 3. The cells are stained after an additional 2 days in culture and are then scored visually the next day. A positive in the assay occurs when the PRO polypeptide treated myocytes are visually smaller on the average or less numerous than the untreated myocytes.

The following PRO polypeptides tested positive in this assay: PRO1760.

EXAMPLE 155: Tissue Expression Distribution

Oligonucleotide probes were constructed from some of the PRO polypeptide-encoding nucleotide sequences shown in the accompanying figures for use in quantitative PCR amplification reactions. The

oligonucleotide probes were chosen so as to give an approximately 200-600 base pair amplified fragment from the 3' end of its associated template in a standard PCR reaction. The oligonucleotide probes were employed in standard quantitative PCR amplification reactions with cDNA libraries isolated from different human adult and/or fetal tissue sources and analyzed by agarose gel electrophoresis so as to obtain a quantitative determination of the level of expression of the PRO polypeptide-encoding nucleic acid in the various tissues tested. Knowledge of the expression pattern or the differential expression of the PRO polypeptide-encoding nucleic acid in various different human tissue types provides a diagnostic marker useful for tissue typing, with or without other tissue-specific markers, for determining the primary tissue source of a metastatic tumor, and the like. These assays provided the following results.

DNA Molecule	Tissues With Significant Expression	Tissues Lacking Significant Expression
DNA19902-1669	HUVEC cells, colon tumor	dendritic cells, lymphoblast cells, heart
DNA23322-1393	uterus, colon tumor, prostate	cartilage
DNA26846-1397	lymphoblast cells	uterus, heart, cartilage
DNA56107-1415	spleen, substantia nigra, colon tumor	cartilage
DNA56406-1704	THP-1 macrophages, uterus, spleen	endothelial cells, prostate, cartilage
DNA56529-1647	liver, kidney, brain	adenocarcionoma, lung, bone marrow
DNA56862-1343	endothelial cells, substantia nigra hippocampus	colon tumor, lymphoblast cells, uterus
DNA57254-1477	kidney	lung, placenta, brain
DNA58730-1607	bone marrow, kidney	lung, brain
DNA58732-1650	lung, bone marrow	brain, liver
DNA58828-1519	adenocarcinoma	lung, retina, small intestine
DNA58852-1637	uterus	colon tumor, heart, brain
DNA59212-1627	uterus	prostate, cartilage, heart
DNA59219-1613	spleen, dendrocytes, prostate, uterus	substantia nigra, colon tumor, heart
DNA59817-1703	bone marrow	lung, small intestine, placenta
DNA60278-1530	prostate, colon tumor	uterus, cartilage
DNA60608-1577	kidney, bone marrow	breast carcinoma, small intestine, lung
DNA60611-1524	breast carcinoma	lung, small intestine, retina
DNA60740-1615	breast carcinoma, adenocarcinoma	lung, small intestine, brain
DNA62809-1531	THP-1 macrophages	uterus, spleen, brain, colon tumor
DNA62815-1576	colon tumor, uterus, prostate	spleen, brain, heart, cartilage
DNA62845-1684	liver, bone marrow	adenocarcinoma, lung, brain
DNA64849-1604	kidney	lung, pancreas, liver, thyroid
DNA64863-1573	lung, brain, kidney, bone marrow	liver, pancreas
DNA64881-1602	uterus	heart, spleen, brain, endothelial cells
DNA64902-1667	urerus	prostate, brain, heart, spleen
DNA64952-1568	lung, brain	pancreas
DNA65403-1565	spleen, dendrocytes, THP-1 macrophages	endothelial cells, colon tumor, lymphoblasts
DNA65408-1578	prostate, spleen, dendrocytes	uterus, heart, substantia nigra
DNA65423-1595	testis	breast carcinoma, retina, small intestine
DNA66512-1564	heart, uterus, prostate, cartilage	endothelial cells
DNA66519-1535	dendrocytes, lymphoblasts, uterus	substantia nigra, prostate, spleen
DNA66521-1583	uterus, heart, hippocampus	cartilage, dendrocytes, spleen
DNA66658-1584	prostate, uterus, hippocampus, spleen	colon tumor, cartilage, heart
DNA66672-1586	spleen	heart, prostate, brain, uterus
DNA66674-1599	uterus, prostate	heart, brain, spleen, cartilage, colon tumor
DNA68836-1656	kidney	lung, brain, bone marrow, liver
DNA68871-1638	uterus, colon tumor, prostate	heart, cartilage, brain, spleen
DNA68880-1676	heart, endothelial cells, brain, uterus	THP-1 macrophages
DNA68885-1678	uterus, colon tumor, prostate	brain, heart, cartilage, endothelial cells
DNA71180-1655	brain	lung, bone marrow, liver, kidney

DNA71184-1634	breast carcinoma, bone marrow, testis	brain, adrenal gland
DNA71234-1651	kidney, bone marrow	lung, brain, placenta
DNA71277-1636	prostate, cartilage, heart, uterus	colon tumor, substantia nigra, endothelial cells
DNA71286-1687	uterus, prostate, brain, cartilage	heart
DNA71883-1660	aortic endothelial cells	lung, retina, small intestine, kidney
DNA73492-1671	breast carcinoma, aortic endothelial cells bone marrow	lung, brain, testis
DNA73734-1680	prostate, spleen	heart, cartilage, brain, uterus
DNA73735-1681	prostate	brain, heart, cartilage, spleen
DNA73736-1657	spleen, substantia nigra, hippocampus, cartilage	prostate, heart, uterus, dendrocytes
DNA73737-1658	uterus	prostate, heart, spleen, cartilage
DNA73742-1662	spleen, uterus, prostate	dendrocytes, colon tumor, endothelial cells
DNA73746-1654	prostate	uterus, heart, brain, cartilage, spleen
DNA73760-1672	breast carcinoma	retina, brain, kidney, liver, testis
DNA76393-1664	endothelial cells, cartilage, uterus	brain, prostate
DNA76398-1699	hippocampus, prostate, THP-1 macrtophages	heart, uterus, spleen, dendrocytes
DNA76399-1700	IM-9 lymphoblasts	prostate, spleen, heart, cartilage, uterus
DNA76522-2500	colon tumor	uterus, prostate, brain, heart, cartilage
DNA77301-1708	brain	lung, small intestine, kidney, liver
DNA77648-1688	retina, breast carcinoma, kidney, liver, bone marrow	brain, lung
DNA77568-1626	brain	lung, liver, placenta, heart
DNA58727-1474	HUVEC, dendrocytes, uterus	substantia nigra, hippocampus, prostate, colon tumor
DNA61185-1646	colon tumor, HUVEC	uterus, dendrocytes, substantia nigra
DNA61608-1606	colon tumor, dendrocytes, spleen, testis	substantia nigra, placenta
DNA66304-1546	prostate, testis	uterus, brain, heart, colon tumor, adrenal gland
DNA71213-1659	brain, spleen, HUVEC, colon tumor	prostate, uterus, heart, cartilage
DNA62812-1594	heart	placenta, testis, uterus, adrenal gland, bone marrow, prostate
DNA66660-1585	colon tumor, HUVEC, testis, placenta, uterus	bone marrow
DNA66669-1597	heart, placenta, adrenal gland, uterus	cartilage, testis, colon tumor, HUVEC, bone marrow, prostate, spleen
DNA68866-1644	testis, colon tumor, prostate, spleen,	cartilage, adrenal gland, HUVEC, placenta
DNA73730-1679	testis, adrenal gland, uterus, prostate, uterus	cartilage, colon tumor, heart, placenta, spleen

Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC):

Table 12

Material	ATCC Dep. No.	Deposit Date
DNA19902-1669	203454	November 3, 1998
DNA26846-1397	203406	October 27, 1998
DNA56107-1415	203405	October 27, 1998
DNA56406-1704	203478	November 17, 1998
DNA56529-1647	203293	September 29, 1998
DNA56531-1648	203286	September 29, 1998
DNA56862-1343	203174	September 1, 1998
DNA57254-1477	203289	September 29, 1998
DNA57841-1522	203458	November 3, 1998
DNA58727-1474	203171	September 1, 1998
DNA58730-1607	203221	September 15, 1998
DNA58732-1650	203290	September 29, 1998
DNA58828-1519	203172	September 1, 1998
DNA58852-1637	203271	September 22, 1998
DNA59212-1627	203245	September 9, 1998
DNA59218-1559	203287	September 29, 1998
DNA59219-1613	203220	September 15, 1998
DNA59586-1520	203288	September 29, 1998
DNA59817-1703	203470	November 17, 1998
DNA60278-1530	203170	September 1, 1998
DNA60608-1577	203126	August 18, 1998
DNA60611-1524	203175	September 1, 1998
DNA60618-1557	203292	September 29, 1998
DNA60740-1615	203456	November 3, 1998
DNA60764-1533	203452	November 10, 1998
DNA60775-1532	203173	September 1, 1998
DNA61185-1646	203464	November 17, 1998
DNA61608-1606	203239	September 9, 1998
DNA62808-1326	203358	October 20, 1998
DNA62809-1531	203237	September 9, 1998
DNA62815-1578	203247	September 9, 1998
DNA62845-1684	203361	October 20, 1998
DNA64842-1632	203278	September 22, 1998
DNA64849-1604	203468	November 17, 1998
DNA64863-1573	203251	September 9, 1998
DNA64881-1602	203240	September 9, 1998
DNA64883-1526	203253	Serptember 9, 1998
DNA64885-1529	203457	November 3, 1998
DNA64886-1601	203241	September 9, 1998
DNA64888-1542	203249	September 9, 1998
DNA64889-1541	203250	September 9, 1998
DNA64897-1628	203216	September 15, 1998
DNA64902-1667	203317	October 6, 1998
DNA64903-1553	203223	September 15, 1998
DNA64905-1558	203233	September 15, 1998
DNA64950-1590	203224	September 15, 1998
DNA64952-1568	203222	September 15, 1998
DNA65402-1540	203252	September 9, 1998
DNA65403-1565	203230	September 15, 1998
DNA65404-1551	203244	September 9, 1998
DNA65405-1547	203476	November 17, 1998
DNA65406-1567	203219	September 15, 1998

	DNA65408-1578	203217	September 15, 1998
	DNA65409-1566	203232	September 15, 1998
	DNA65410-1569	203231	September 15, 1998
	DNA65423-1595	203227	September 15, 1998
	DNA66304-1546	203321	October 6, 1998
5	DNA66511-1411	203228	September 15, 1998
	DNA66512-1564	203218	September 15, 1998
	DNA66519-1535	203236	September 15, 1998
	DNA66520-1536	203226	September 15, 1998
	DNA66521-1583	203225	September 15, 1998
10	DNA66526-1616	203246	September 9, 1998
	DNA66658-1584	203229	September 15, 1998
	DNA66659-1593	203269	September 22, 1998
	DNA66663-1598	203268	September 22, 1998
	DNA66669-1597	203272	September 22, 1998
15	DNA66672-1586	203265	September 22, 1998
	DNA66674-1599	203281	September 22, 1998
	DNA66675-1587	203282	September 22, 1998
	DNA67962-1649	203291	September 29, 1998
	DNA68836-1656	203455	November 3, 1998
20	DNA68864-1629	203276	September 22, 1998
	DNA68866-1644	203283	September 22, 1998
	DNA68871-1638	203280	September 22, 1998
	DNA68874-1622	203277	September 22, 1998
	DNA68880-1676	203319	October 6, 1998
25	DNA68885-1570	203311	October 6, 1998
	DNA71166-1685	203355	October 20, 1998
	DNA71169-1709	203467	November 17, 1998
	DNA71180-1655	203403	October 27, 1998
	DNA71184-1634	203266	September 22, 1998
30	DNA71213-1659	203401	October 27, 1998
	DNA71234-1651	203402	October 27, 1998
	DNA71277-1636	203285	September 22, 1998
	DNA71282-1668	203312	October 6, 1998
	DNA71286-1604	203357	October 20, 1998
35	DNA71883-1660	203475	November 17, 1998
	DNA73401-1633	203273	September 22, 1998
	DNA73492-1671	203324	October 6, 1998
	DNA73727-1673	203459	November 3, 1998
	DNA73730-1679	203320	October 6, 1998
40	DNA73734-1680	203363	October 20, 1998
	DNA73735-1681	203356	October 20, 1998
	DNA73736-1657	203466	November 17, 1998
	DNA73737-1658	203412	October 27, 1998
	DNA73739-1645	203270	September 22, 1998
45	DNA73742-1662	203316	October 6, 1998
	DNA73744-1665	203322	October 6, 1998
	DNA73746-1654	203411	October 27, 1998
	DNA73760-1672	203314	October 6, 1998
	DNA76396-1698	203471	November 17, 1998
50	DNA76398-1699	203474	November 17, 1998
	DNA76399-1700	203472	November 17, 1998
	DNA76401-1683	203360	October 20, 1998
	DNA76510-2504	203477	November 17, 1998
	DNA76522-2500	203469	November 17, 1998
55	DNA76529-1666	203315	October 6, 1998
	DNA76531-1701	203465	November 17, 1998
	DNA76532-1702	203473	November 17, 1998
	DNA76538-1670	203313	October 6, 1998

DNA76541-1675	203409	October 27, 1998
DNA77301-1708	203407	October 27, 1998
DNA77303-2502	203479	November 17, 1998
DNA77648-1688	203408	October 27, 1998
DNA77652-2505	203480	November 17, 1998
DNA83500-2506	203391	October 29, 1998
DNA77568-1626	203134	August 18, 1998
DNA23322-1393	203400	October 27, 1998
DNA59814-1486	203359	October 20, 1998
DNA62812-1594	203248	September 9, 1998
DNA66660-1585	203279	September 22, 1998
DNA76393-1664	203323	October 6, 1998

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to 886 OG 638).

The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.